=> file caplus; d que l2
FILE 'CAPLUS' ENTERED AT 15:51:42 ON 18 APR 2003
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FILE COVERS 1907 - 18 Apr 2003 VOL 138 ISS 17
FILE LAST UPDATED: 17 Apr 2003 (20030417/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L2 3 SEA FILE=CAPLUS ABB=ON PLU=ON BRACEGIRDLE P?/AU AND GORRINGE A?/AU

=> file medline; d que l39
FILE 'MEDLINE' ENTERED AT 15:51:49 ON 18 APR 2003

FILE LAST UPDATED: 17 APR 2003 (20030417/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L39 1 SEA FILE=MEDLINE ABB=ON PLU=ON GORRINGE A?/AU AND BRACEGIRDLE P?/AU

=> file embase; d que l63
FILE 'EMBASE' ENTERED AT 15:51:59 ON 18 APR 2003

FILE COVERS 1974 TO 17 Apr 2003 (20030417/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L63 1 SEA FILE=EMBASE ABB=ON PLU=ON BRACEGIRDLE P?/AU AND GORRINGE

A?/AU

=> file biosis; d que l93
FILE 'BIOSIS' ENTERED AT 15:52:06 ON 18 APR 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 16 April 2003 (20030416/ED)

L91 34 SEA FILE=BIOSIS ABB=ON PLU=ON GORRINGE A?/AU
L92 6 SEA FILE=BIOSIS ABB=ON PLU=ON BRACEGIRDLE P?/AU
L93 3 SEA FILE=BIOSIS ABB=ON PLU=ON L91 AND L92

=> file wpid; d que l102
FILE 'WPIDS' ENTERED AT 15:52:12 ON 18 APR 2003
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FILE LAST UPDATED: 16 APR 2003 <20030416/UP>
MOST RECENT DERWENT UPDATE: 200325 <200325/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
GUIDES, PLEASE VISIT:
http://www.derwent.com/userguides/dwpi_guide.html <<<

L102 2 SEA FILE=WPIDS ABB=ON PLU=ON BRACEGIRDLE P?/AU AND GORRINGE
A?/AU

=> dup rem l2 l39 l63 l93 l102
FILE 'CAPLUS' ENTERED AT 15:52:31 ON 18 APR 2003
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FILE 'MEDLINE' ENTERED AT 15:52:31 ON 18 APR 2003

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FILE 'WPIDS' ENTERED AT 15:52:31 ON 18 APR 2003
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PROCESSING COMPLETED FOR L2
PROCESSING COMPLETED FOR L39
PROCESSING COMPLETED FOR L63
PROCESSING COMPLETED FOR L93
PROCESSING COMPLETED FOR L102
L120 5 DUP REM L2 L39 L63 L93 L102 (5 DUPLICATES REMOVED)
ANSWERS '1-3' FROM FILE CAPLUS
ANSWERS '4-5' FROM FILE BIOSIS

=> d ibib ab l120 1-5

L120 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:754696 CAPLUS
DOCUMENT NUMBER: 137:293520
TITLE: Antibody-containing sera for identifying Pathogenic and commensal bacteria antigens as vaccines
INVENTOR(S): Robinson, Andrew; **Gorringe, Andrew Richard;** Hudson, Michael John; **Bracegirdle, Philippa;** West, David McKay; Oliver, Kerry Jane; Kroll, John Simon; Langford, Paul Richard
PATENT ASSIGNEE(S): Microbiological Research Authority, UK; Imperial College Innovations Limited
SOURCE: PCT Int. Appl., 310 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002077648	A2	20021003	WO 2002-GB1399	20020322

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-7219 A 20010322
AB The invention provides methods of screening commensal and pathogenic bacteria for previously unidentified vaccine antigens, based upon identifying polypeptide antigens that bind to sera raised against commensal bacterial proteins. Also provided are vaccine compns. and methods of prepg. vaccine compns. comprising the antigens identified by the screening methods. Antigens and uses thereof are also described.

L120 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:489704 CAPLUS
DOCUMENT NUMBER: 138:226458
TITLE: Neisseria lactamica protects against experimental meningococcal infection
AUTHOR(S): Oliver, Kerry J.; Reddin, Karen M.; **Bracegirdle, Philippa;** Hudson, Michael J.; Borrow, Ray; Feavers, Ian M.; Robinson, Andrew; Cartwright, Keith;

Gorringe, Andrew R.
CORPORATE SOURCE: Centre for Applied Microbiology and Research, Salisbury, SP4 0JG, UK
SOURCE: Infection and Immunity (2002), 70(7), 3621-3626
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Immunol. and epidemiol. evidence suggests that the development of natural immunity to meningococcal disease results from colonization of the nasopharynx by commensal Neisseria spp., particularly with N. lactamica. We report here that immunization with N. lactamica killed whole cells, outer membrane vesicles, or outer membrane protein (OMP) pools and protected mice against lethal challenge by a no. of diverse serogroup B and C meningococcal isolates in a model of bacteremic infection. Sera raised to N. lactamica killed whole cells, OMPs, or protein pools were found to cross-react with meningococcal isolates of a diverse range of genotypes and phenotypes. The results confirm the potential of N. lactamica to form the basis of a vaccine against meningococcal disease.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L120 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 2000:608607 CAPLUS
DOCUMENT NUMBER: 133:213155
TITLE: Neisserial vaccine compositions and methods
INVENTOR(S): Robinson, Andrew; **Gorringe, Andrew Richard**; Hudson, Michael John; **Bracegirdle, Philippa**; Kroll, John Simon; Cartwright, Keith
PATENT ASSIGNEE(S): Microbiological Research Authority, UK; Imperial College School of Science, Technology and Medicine; Public Health Laboratory Service Board
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050074	A2	20000831	WO 2000-GB624	20000222
WO 2000050074	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1154791	A2	20011121	EP 2000-905182	20000222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537352	T2	20021105	JP 2000-600684	20000222
US 2003026809	A1	20030206	US 2001-942583	20010831
US 2003021812	A1	20030130	US 2002-185769	20020701

PRIORITY APPLN. INFO.: GB 1999-4028 A 19990222
GB 1999-22561 A 19990923
WO 2000-GB624 W 20000222

US 2001-914041 A1 20010822

AB Methods and compns. for the treatment of microbial infection, and in particular meningococcal disease, comprise a commensal Neisseria or an ext. of a commensal Neisseria. Further methods and compns. comprise commensal Neisseria which express genes from virulent strains of Neisseria and/or heterologous gene products from non-neisserial sources. Such compns. are used in vaccine prepns. for the treatment of microbial infection.

L120 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:2701 BIOSIS
DOCUMENT NUMBER: PREV200100002701
TITLE: Neisseria lactamica provides a cross-reactive vaccine against meningococcal disease.
AUTHOR(S): **Bracegirdle, P. (1)**; Oliver, K. (1); Reddin, K. (1); Cartwright, K.; Feavers, I.; Borrow, R.; Hudson, M. (1); Robinson, A. (1); **Gorringe, A. (1)**
CORPORATE SOURCE: (1) Ctr. for Applied Microbiol. and Res., Salisbury UK
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 248. print. Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L120 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:474832 BIOSIS
DOCUMENT NUMBER: PREV200000474832
TITLE: Neisseria lactamica as a vaccine against meningococcal disease.
AUTHOR(S): **Gorringe, A. R. (1)**; **Bracegirdle, P. (1)**; Oliver, K. (1); Reddin, K. (1); Cartwright, K.; Feavers, I.; Fox, A.; Robinson, A. (1)
CORPORATE SOURCE: (1) Ctr. for Applied Microbiol. and Res., Salisbury UK
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1999) Vol. 39, pp. 362. cd-rom. Meeting Info.: 39th Interscience Conference on Antimicrobial Agents and Chemotherapy San Francisco, California, USA September 26-29, 1999 American Society for Microbiology
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

```
=> file reg; d rn cn l19; d rn cn l20
FILE 'REGISTRY' ENTERED AT 15:53:11 ON 18 APR 2003
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STRUCTURE FILE UPDATES:   17 APR 2003  HIGHEST RN 503414-07-1
DICTIONARY FILE UPDATES:  17 APR 2003  HIGHEST RN 503414-07-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L19  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   9054-89-1  REGISTRY
CN   Dismutase, superoxide (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Artolasi
CN   Cuprein
CN   CZSOD
CN   Dismuzyme Plus
CN   E.C. 1.15.1.1
CN   Erisod
CN   Erythrocupreins
CN   Hemocuprein
CN   Ontosein
CN   Orgotein
CN   Orgoteins
CN   Ormetein
CN   Oximorm
CN   Palosein
CN   Peroxide dismutase
CN   Peroxinorm
CN   Superoxide dismutase
CN   Superphycodismutase


L20  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   183600-13-7  REGISTRY
CN   Antigen (Neisseria meningitidis clone pNP2202 22-kilodalton precursor)
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   1: PN: WO0071725 FIG: 29 claimed protein
CN   NspA protein (Neisseria meningitidis strain 608B clone pNP2202 gene
     nspA precursor)
```

CN Outer membrane protein NspA (Neisseria meningitidis strain 608B clone pNP2202 precursor)
CN Outer membrane protein NspA (Neisseria meningitidis clone pNP2202 gene nspA precursor)
CN Protein (Neisseria meningitidis strain 608B gene nspA)
CN Surface protein A (Neisseria meningitidis strain M986 gene nspA)
CN Surface protein A (Neisseria meningitidis strain NGP165 gene nspA)
CN Surface protein A (Neisseria meningitidis strain NG6/88 gene nspA)

=> file caplus; d que l28
FILE 'CAPLUS' ENTERED AT 15:53:35 ON 18 APR 2003
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FILE COVERS 1907 - 18 Apr 2003 VOL 138 ISS 17
FILE LAST UPDATED: 17 Apr 2003 (20030417/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L3	6183	SEA FILE=CAPLUS ABB=ON PLU=ON	NEISSERIA/CW
L4	1521	SEA FILE=CAPLUS ABB=ON PLU=ON	N (W) (CINEREA OR ELONGATA OR ?FLAV? OR LACTAMICA OR MENINGITIDIS OR POLYSACCHAREA OR SICCA)
L5	32582	SEA FILE=CAPLUS ABB=ON PLU=ON	VACCINES/CT
L6	5732	SEA FILE=CAPLUS ABB=ON PLU=ON	IMMUNIZATION/CT
L7	10707	SEA FILE=CAPLUS ABB=ON PLU=ON	IMMUNOSTIMULANTS/CT
L8	2014	SEA FILE=CAPLUS ABB=ON PLU=ON	IMMUNOSTIMULATION/CT
L12	2208	SEA FILE=CAPLUS ABB=ON PLU=ON	MENINGITIS/CT
L19	1	SEA FILE=REGISTRY ABB=ON PLU=ON	9054-89-1/RN
L20	1	SEA FILE=REGISTRY ABB=ON PLU=ON	"NSPA PROTEIN (NEISSERIA MENINGITIDIS STRAIN 608B CLONE PNP2202 GENE NSPA PRECURSOR)"/CN
L21	19223	SEA FILE=CAPLUS ABB=ON PLU=ON	TRANSFERRIN
L22	23096	SEA FILE=CAPLUS ABB=ON PLU=ON	CZSOD OR L19
L23	1026486	SEA FILE=CAPLUS ABB=ON PLU=ON	CU OR COPPER
L24	666014	SEA FILE=CAPLUS ABB=ON PLU=ON	ZN OR ZINC
L25	24	SEA FILE=CAPLUS ABB=ON PLU=ON	NSPA OR L20
L27	3979	SEA FILE=CAPLUS ABB=ON PLU=ON	PORINS/CT
L28	14	SEA FILE=CAPLUS ABB=ON PLU=ON	(L3 OR L4) AND (L5 OR L6 OR L7 OR L8) AND L12 AND ((L21 OR L22 OR L23 OR L24 OR L25) OR L27)

=> file medline; d que l42; d que l47
FILE 'MEDLINE' ENTERED AT 15:53:45 ON 18 APR 2003

FILE LAST UPDATED: 17 APR 2003 (20030417/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L30        4731 SEA FILE=MEDLINE ABB=ON  PLU=ON  NEISSERIA MENINGITIDIS+NT/CT
L31       86770 SEA FILE=MEDLINE ABB=ON  PLU=ON  VACCINES+NT/CT
L32       83822 SEA FILE=MEDLINE ABB=ON  PLU=ON  IMMUNIZATION+NT/CT
L33       18128 SEA FILE=MEDLINE ABB=ON  PLU=ON  ADJUVANTS, IMMUNOLOGIC/CT
L34         598 SEA FILE=MEDLINE ABB=ON  PLU=ON  TRANSFERRIN BINDING
L35           8 SEA FILE=MEDLINE ABB=ON  PLU=ON  NSPA PROTEIN/CN
L36       55061 SEA FILE=MEDLINE ABB=ON  PLU=ON  CU OR COPPER
L37       59815 SEA FILE=MEDLINE ABB=ON  PLU=ON  ZN OR ZINC
L40        3191 SEA FILE=MEDLINE ABB=ON  PLU=ON  L30/MAJ
L41       91283 SEA FILE=MEDLINE ABB=ON  PLU=ON  L31/MAJ OR L32/MAJ OR L33/MAJ

L42          10 SEA FILE=MEDLINE ABB=ON  PLU=ON  L40 AND L41 AND (L34 OR L35
                OR L36 OR L37)



L30        4731 SEA FILE=MEDLINE ABB=ON  PLU=ON  NEISSERIA MENINGITIDIS+NT/CT
L31       86770 SEA FILE=MEDLINE ABB=ON  PLU=ON  VACCINES+NT/CT
L32       83822 SEA FILE=MEDLINE ABB=ON  PLU=ON  IMMUNIZATION+NT/CT
L33       18128 SEA FILE=MEDLINE ABB=ON  PLU=ON  ADJUVANTS, IMMUNOLOGIC/CT
L34         598 SEA FILE=MEDLINE ABB=ON  PLU=ON  TRANSFERRIN BINDING
L35           8 SEA FILE=MEDLINE ABB=ON  PLU=ON  NSPA PROTEIN/CN
L36       55061 SEA FILE=MEDLINE ABB=ON  PLU=ON  CU OR COPPER
L37       59815 SEA FILE=MEDLINE ABB=ON  PLU=ON  ZN OR ZINC
L44       29283 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIBODIES, BACTERIAL/CT
L45       25233 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIGENS, BACTERIAL/CT
L46       24551 SEA FILE=MEDLINE ABB=ON  PLU=ON  L44/MAJ OR L45/MAJ
L47          10 SEA FILE=MEDLINE ABB=ON  PLU=ON  L30 AND (L31 OR L32 OR L33)
                AND (L34 OR L35 OR L36 OR L37) AND L46


=> s l42 or l47
L121         17 L42 OR L47

=> file embase; d que l64; d que l70; d que l76
FILE 'EMBASE' ENTERED AT 15:54:37 ON 18 APR 2003
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 FILE COVERS 1974 TO 17 Apr 2003 (20030417/ED)

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L49       14577 SEA FILE=EMBASE ABB=ON  PLU=ON  NEISSERIA
L50       25009 SEA FILE=EMBASE ABB=ON  PLU=ON  MENINGITIS+NT/CT
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L51       12467 SEA FILE=EMBASE ABB=ON  PLU=ON  VACCINE/CT
L52       68586 SEA FILE=EMBASE ABB=ON  PLU=ON  IMMUNIZATION+NT/CT
L53        1093 SEA FILE=EMBASE ABB=ON  PLU=ON  IMMUNOSTIMULATING AGENT/CT
L54        2691 SEA FILE=EMBASE ABB=ON  PLU=ON  TRANSFERRIN BINDING OR TBP?
L56           1 SEA FILE=EMBASE ABB=ON  PLU=ON  CZSOD
L57       54651 SEA FILE=EMBASE ABB=ON  PLU=ON  CU OR COPPER
L58       64140 SEA FILE=EMBASE ABB=ON  PLU=ON  ZN OR ZINC
L59          13 SEA FILE=EMBASE ABB=ON  PLU=ON  NSPA
L64           4 SEA FILE=EMBASE ABB=ON  PLU=ON  L49 AND L50 AND (L51 OR L52 OR
                L53) AND (L54 OR (L56 OR L57 OR L58 OR L59))


L49       14577 SEA FILE=EMBASE ABB=ON  PLU=ON  NEISSERIA
L50       25009 SEA FILE=EMBASE ABB=ON  PLU=ON  MENINGITIS+NT/CT
L51       12467 SEA FILE=EMBASE ABB=ON  PLU=ON  VACCINE/CT
L52       68586 SEA FILE=EMBASE ABB=ON  PLU=ON  IMMUNIZATION+NT/CT
L53        1093 SEA FILE=EMBASE ABB=ON  PLU=ON  IMMUNOSTIMULATING AGENT/CT
L54        2691 SEA FILE=EMBASE ABB=ON  PLU=ON  TRANSFERRIN BINDING OR TBP?
L55        4331 SEA FILE=EMBASE ABB=ON  PLU=ON  OUTER MEMBRANE PROTEIN/CT
L56           1 SEA FILE=EMBASE ABB=ON  PLU=ON  CZSOD
L57       54651 SEA FILE=EMBASE ABB=ON  PLU=ON  CU OR COPPER
L58       64140 SEA FILE=EMBASE ABB=ON  PLU=ON  ZN OR ZINC
L59          13 SEA FILE=EMBASE ABB=ON  PLU=ON  NSPA
L67        1314 SEA FILE=EMBASE ABB=ON  PLU=ON  MENINGOCOCCUS VACCINE/CT
L68         802 SEA FILE=EMBASE ABB=ON  PLU=ON  L67/MAJ
L69           8 SEA FILE=EMBASE ABB=ON  PLU=ON  L49 AND L50 AND (L51 OR L52 OR
                L53) AND (L54 OR L55 OR L56 OR L57 OR L58 OR L59) AND (L67 OR
                L68)
L70           6 SEA FILE=EMBASE ABB=ON  PLU=ON  L69 NOT (FURTIVE OR EPIDEMIOLOG
                Y)/TI


L49       14577 SEA FILE=EMBASE ABB=ON  PLU=ON  NEISSERIA
L59          13 SEA FILE=EMBASE ABB=ON  PLU=ON  NSPA
L76           8 SEA FILE=EMBASE ABB=ON  PLU=ON  L59 AND L49


=> s l64 or l70 or l76
L122         14 L64 OR L70 OR L76

=> file biosis; d que l84; d que l96; d que l97; d que l98; d que l101
FILE 'BIOSIS' ENTERED AT 15:55:59 ON 18 APR 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 16 April 2003 (20030416/ED)


L84           0 SEA FILE=BIOSIS ABB=ON  PLU=ON  CZSOD


L79       15416 SEA FILE=BIOSIS ABB=ON  PLU=ON  NEISSERIA OR N (W) (CINEREA OR
                LACTAMICA OR ELONGATA OR ?FLAV? OR POLYSACCH? OR SICCA OR
                MUCOSA)
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L80       18301 SEA FILE=BIOSIS ABB=ON  PLU=ON  MENINGITIS
L81      175445 SEA FILE=BIOSIS ABB=ON  PLU=ON  VACCIN? OR IMMUNIZ? OR
                IMMUNOSTIMULA? OR (SENSITIZ? OR STIMULAT?) (1A) IMMUNO? OR
                IMMUNOMODULAT? OR IMMUNOPOTENTIAT? OR IMMUNOACTIVAT?
L87          17 SEA FILE=BIOSIS ABB=ON  PLU=ON  NSPA
L96           1 SEA FILE=BIOSIS ABB=ON  PLU=ON  L79 AND L80 AND L81 AND L87


L79       15416 SEA FILE=BIOSIS ABB=ON  PLU=ON  NEISSERIA OR N (W) (CINEREA OR
                LACTAMICA OR ELONGATA OR ?FLAV? OR POLYSACCH? OR SICCA OR
                MUCOSA)
L80       18301 SEA FILE=BIOSIS ABB=ON  PLU=ON  MENINGITIS
L81      175445 SEA FILE=BIOSIS ABB=ON  PLU=ON  VACCIN? OR IMMUNIZ? OR
                IMMUNOSTIMULA? OR (SENSITIZ? OR STIMULAT?) (1A) IMMUNO? OR
                IMMUNOMODULAT? OR IMMUNOPOTENTIAT? OR IMMUNOACTIVAT?
L88        2546 SEA FILE=BIOSIS ABB=ON  PLU=ON  PORIN
L97           8 SEA FILE=BIOSIS ABB=ON  PLU=ON  L79 AND L80 AND L81 AND L88


L79       15416 SEA FILE=BIOSIS ABB=ON  PLU=ON  NEISSERIA OR N (W) (CINEREA OR
                LACTAMICA OR ELONGATA OR ?FLAV? OR POLYSACCH? OR SICCA OR
                MUCOSA)
L80       18301 SEA FILE=BIOSIS ABB=ON  PLU=ON  MENINGITIS
L81      175445 SEA FILE=BIOSIS ABB=ON  PLU=ON  VACCIN? OR IMMUNIZ? OR
                IMMUNOSTIMULA? OR (SENSITIZ? OR STIMULAT?) (1A) IMMUNO? OR
                IMMUNOMODULAT? OR IMMUNOPOTENTIAT? OR IMMUNOACTIVAT?
L85       82942 SEA FILE=BIOSIS ABB=ON  PLU=ON  CU OR COPPER
L86       93271 SEA FILE=BIOSIS ABB=ON  PLU=ON  ZN OR ZINC
L98           0 SEA FILE=BIOSIS ABB=ON  PLU=ON  L79 AND L80 AND L81 AND (L85
                OR L86)


L79       15416 SEA FILE=BIOSIS ABB=ON  PLU=ON  NEISSERIA OR N (W) (CINEREA OR
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L80       18301 SEA FILE=BIOSIS ABB=ON  PLU=ON  MENINGITIS
L81      175445 SEA FILE=BIOSIS ABB=ON  PLU=ON  VACCIN? OR IMMUNIZ? OR
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L100          4 SEA FILE=BIOSIS ABB=ON  PLU=ON  L79 AND L80 AND L81 AND L99
L101          2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L100 AND (RATIONAL OR LIBRARY)/
                TI


=> s l96 or l97 or l101
L123         11 L96 OR L97 OR L101

=> file wpid; d que l111; d que l113; d que l114; d que l118; d que l119
FILE 'WPIDS' ENTERED AT 15:56:41 ON 18 APR 2003
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L113 2 SEA FILE=WPIDS ABB=ON PLU=ON L112 AND MENING?/TI

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L105 391 SEA FILE=WPIDS ABB=ON PLU=ON TRANSFERRIN BINDING OR TBP?
L109 13 SEA FILE=WPIDS ABB=ON PLU=ON L103 AND L104 AND L105
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L115 17 SEA FILE=WPIDS ABB=ON PLU=ON L110 AND NEISSERIA/TI
L116 11 SEA FILE=WPIDS ABB=ON PLU=ON L115 NOT GONOR?/TI

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L106        332 SEA FILE=WPIDS ABB=ON  PLU=ON  OUTER MEMBRANE (1A) PROTEIN
L110         48 SEA FILE=WPIDS ABB=ON  PLU=ON  L103 AND L104 AND L106
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PROCESSING COMPLETED FOR L28
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                ANSWERS '29-35' FROM FILE EMBASE
                ANSWERS '36-45' FROM FILE BIOSIS
                ANSWERS '46-57' FROM FILE WPIDS

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L125 ANSWER 1 OF 57     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2002622017     MEDLINE
DOCUMENT NUMBER:    22267096   PubMed ID: 12379678
TITLE:              Sequential immunization with vesicles prepared from
                    heterologous Neisseria meningitidis strains elicits broadly
                    protective serum antibodies to group B strains.
AUTHOR:             Moe Gregory R; Zuno-Mitchell Patricia; Hammond Samantha N;
                    Granoff Dan M
CORPORATE SOURCE:   Children's Hospital Oakland Research Institute, Oakland,
                    California 94609-1673, USA.
CONTRACT NUMBER:    AI46464 (NIAID)
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R01 AI45642 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (2002 Nov) 70 (11) 6021-31.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20021017
Last Updated on STN: 20021213
Entered Medline: 20021108

AB The capsular polysaccharide of Neisseria meningitidis group B is an autoantigen, whereas noncapsular antigens are highly variable. These factors present formidable challenges for development of a broadly protective and safe group B vaccine. Mice and guinea pigs were sequentially immunized with three doses of micovesicles or outer membrane vesicles prepared from three meningococcal strains that were each antigenically heterologous with respect to the two major porin proteins, PorA and PorB, and the group capsular polysaccharide. The resulting antisera conferred passive protection against meningococcal group B bacteremia in infant rats and elicited complement-mediated bactericidal activity against genetically diverse group B strains that were either homologous or heterologous with respect to PorA of the strains used to prepare the vaccine. By using knockout strains, a portion of the bactericidal antibody was directed against the highly conserved protein, neisserial surface protein A (NspA). Further, an anti-NspA monoclonal antibody elicited by the sequential immunization was highly bactericidal against strains that were previously shown to be resistant to bacteriolysis by anti-NspA antibodies produced by immunization with recombinant NspA. Sequential immunization with heterologous vesicle preparations offers a novel approach to eliciting broadly protective immunity against N. meningitidis strains. An NspA-based vaccine prepared from protein expressed by Neisseria also may be more effective than the corresponding recombinant protein made in Escherichia coli.

L125 ANSWER 2 OF 57 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002439528 MEDLINE
DOCUMENT NUMBER: 22185255 PubMed ID: 12197384
TITLE: [Induction of the anti-meningitis immunity with synthetic peptides. III. Immunoactive synthetic fragments of NspA protein from Neisseria meningitidis].
Induktsiia protivomeningitnogo immuniteta s pomoshch'iu sinteticheskikh peptidov. III. Immunoaktivnye sinteticheskie fragmenty belka NspA iz Neisseria meningitidis.
AUTHOR: Koroev D O; Oboznaia M B; Zhmak M N; Volkova T D; Titova M A; Kotel'nikova O V; Lakhtina O E; Vol'pina O M; Nesmeianov V A; Alliluev A P; Ivanov V T
CORPORATE SOURCE: Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, ul. Miklukho-Maklaya 16/10, GSP Moscow, 117997 Russia.. koroev@ibch.ru
SOURCE: BIOORGANICHESKAIA KHIMIIA, (2002 Jul-Aug) 28 (4) 291-7.
Journal code: 7804941. ISSN: 0132-3423.
PUB. COUNTRY: Russia: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020829
Last Updated on STN: 20020925
Entered Medline: 20020924

AB Four potentially immunoactive peptide fragments of the NspA protein from the outer membrane of the bacterium Neisseria meningitidis were synthesized in order to create a synthetic vaccine against the meningococcal infection by the serogroup B bacterium. Mice of various lines were immunized with the free peptides nonconjugated with a protein carrier. All the synthetic peptides were shown to induce the production of the antipeptide antibodies in mice. A peptide capable of inducing a decrease in the number of bacteria in blood and the protection of infected animals from death was found in the experiments on the protection of the animals infected with two strains of the Neisseria meningitidis serogroup B. The English version of the paper: Russian Journal of Bioorganic Chemistry, 2002, vol. 28, no. 4; see also http://www.maik.ru.

L125 ANSWER 3 OF 57 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001371335 MEDLINE
DOCUMENT NUMBER: 21246678 PubMed ID: 11349041
TITLE: Functional activity of anti-Neisserial surface protein A monoclonal antibodies against strains of Neisseria meningitidis serogroup B.
AUTHOR: Moe G R; Zuno-Mitchell P; Lee S S; Lucas A H; Granoff D M
CORPORATE SOURCE: Children's Hospital Oakland Research Institute, California 94609, USA.
CONTRACT NUMBER: AI25008 (NIAID)
AI46464 (NIAID)
RO1 AI45642 (NIAID)
RR01271 (NCRR)
SOURCE: INFECTION AND IMMUNITY, (2001 Jun) 69 (6) 3762-71.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB Neisserial surface protein A (NspA) is currently being investigated with humans as a candidate vaccine for the prevention of meningococcal disease. Although NspA is highly conserved, the ability of anti-NspA antibodies to bind to or elicit complement-mediated bactericidal activity against diverse Neisseria meningitidis serogroup B strains is controversial. To evaluate strain differences in NspA surface accessibility and susceptibility to bactericidal activity, we prepared murine immunoglobulin G2a anti-NspA monoclonal antibodies (MAbs) and evaluated their functional activity against 10 genetically diverse N. meningitidis serogroup B strains. By colony Western blot, all 10 strains expressed NspA as detected by one or more MAbs. By flow cytometry, two MAbs were found to bind to the bacterial surface of 6 of the 10 strains. In addition, two strains showed variable NspA surface accessibility for the MAbs despite being uniformly positive for NspA expression by colony Western blotting. Only 4 of the 10 strains were susceptible to anti-NspA complement-mediated bacteriolysis. Passively administered MAb protected infant rats from developing bacteremia after challenge with N. meningitidis serogroup B strain 8047 (surface binding positive, susceptible to anti-NspA bacteriolysis), was poorly protective against strain BZ232 (surface binding variable, resistant to bacteriolysis), and did not protect against strain M986 (surface binding negative, resistant to bacteriolysis). Finally, NspA does not appear to be critical for causing bacteremia, as an NspA knockout from strain 8047 was highly virulent in infant rats. Taken together, these findings suggest that an NspA-based vaccine will need to incorporate additional antigens to elicit broad protection against N.

meningitidis serogroup B.

L125 ANSWER 4 OF 57 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001285380 MEDLINE
DOCUMENT NUMBER: 21116971 PubMed ID: 11179327
TITLE: Recombinant Neisseria meningitidis **transferrin binding** protein A protects against experimental meningococcal infection.
AUTHOR: West D; Reddin K; Matheson M; Heath R; Funnell S; Hudson M; Robinson A; Gorringe A
CORPORATE SOURCE: Centre for Applied Microbiology and Research, Salisbury SP4 0JG, United Kingdom.
SOURCE: INFECTION AND IMMUNITY, (2001 Mar) 69 (3) 1561-7. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20021218
Entered Medline: 20010524

AB To better characterize the vaccine potential of Neisseria meningitidis **transferrin binding** proteins (Tbps), we have overexpressed TbpA and TbpB from Neisseria meningitidis isolate K454 in Escherichia coli. The ability to bind human transferrin was retained by both recombinant proteins, enabling purification by affinity chromotography. The recombinant Tbps were evaluated individually and in combination in a mouse intraperitoneal-infection model to determine their ability to protect against meningococcal infection and to induce cross-reactive and bactericidal antibodies. For the first time, TbpA was found to afford protection against meningococcal challenge when administered as the sole immunogen. In contrast to the protection conferred by TbpB, this protection extended to a serogroup C isolate and strain B16B6, a serogroup B isolate with a lower-molecular-weight TbpB than that from strain K454. However, serum from a TbpB-immunized rabbit was found to be significantly more bactericidal than that from a TbpA-immunized animal. Our evidence demonstrates that TbpA used as a vaccine antigen may provide protection against a wider range of meningococcal strains than does TbpB alone. This protection appears not to be due to complement-mediated lysis and indicates that serum bactericidal activity may not always be the most appropriate predictor of efficacy for protein-based meningococcal vaccines.

L125 ANSWER 5 OF 57 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001043724 MEDLINE
DOCUMENT NUMBER: 20457000 PubMed ID: 11000456
TITLE: Candidate Neisseria meningitidis NspA vaccine.
AUTHOR: Martin D; Brodeur B R; Hamel J; Couture F; de Alwis U; Lian Z; Martin S; Andrews D; Ellis R W
CORPORATE SOURCE: Unite de Recherche en Vaccinologie, Centre Hospitalier Universitaire de Quebec, Pavillon CHUL et Universite Laval, Sainte-Foy, G1V 4G2, Quebec, Canada.. denis.martin@crchul.ulaval.ca
SOURCE: JOURNAL OF BIOTECHNOLOGY, (2000 Sep 29) 83 (1-2) 27-31. Journal code: 8411927. ISSN: 0168-1656.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001204

AB The highly conserved NspA protein has been found in the outer membrane of every Neisseria meningitidis strain tested so far. Two monoclonal antibodies (MAbs) directed against this protein were used to demonstrate that biologically important epitopes of the NspA protein are exposed at the surface of serologically distinct meningococcal strains. Analysis of sera collected from mice that survived a deadly meningococcal challenge following immunization with recombinant NspA protein (rNspA) revealed the presence of cross-reactive antibodies which efficiently attached to and killed the four serogroup B strains tested. These data are additional proof that the NspA protein is exposed at the surface of intact meningococcal cells, which is an important characteristic for a vaccine candidate.

L125 ANSWER 6 OF 57 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2000002540 MEDLINE
DOCUMENT NUMBER: 20002540 PubMed ID: 10531214
TITLE: Differences in surface expression of NspA among Neisseria meningitidis group B strains.
AUTHOR: Moe G R; Tan S; Granoff D M
CORPORATE SOURCE: Children's Hospital Oakland Research Institute, Oakland, California 94609, USA.
SOURCE: INFECTION AND IMMUNITY, (1999 Nov) 67 (11) 5664-75.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991116

AB NspA is a highly conserved membrane protein that is reported to elicit protective antibody responses against Neisseria meningitidis serogroups A, B and C in mice (D. Martin, N. Cadieux, J. Hanel, and B. R. Brodeur, J. Exp. Med. 185:1173-1183, 1997). To investigate the vaccine potential of NspA, we produced mouse anti-recombinant NspA (rNspA) antisera, which were used to evaluate the accessibility of NspA epitopes on the surface of different serogroup B strains by an immunofluorescence flow cytometric assay and by susceptibility to antibody-dependent, complement-mediated bacteriolysis. Among 17 genetically diverse strains tested, 11 (65%) were positive for NspA cell surface epitopes and 6 (35%) were negative. All six negative strains also were resistant to bactericidal activity induced by the anti-rNspA antiserum. In contrast, of the 11 NspA surface-positive strains, 8 (73%; $P < 0.05$) were killed by the antiserum and complement. In infant rats challenged with one of these eight strains, the anti-rNspA antiserum conferred protection against bacteremia, whereas the antiserum failed to protect rats challenged by one of the six NspA cell surface-negative strains. Neither NspA expression nor protein sequence accounted for differences in NspA surface accessibility, since all six negative strains expressed NspA in outer membrane preparations and since their predicted NspA amino acid sequences were 99 to 100% identical to those of three representative positive strains. However, the six NspA cell surface-negative strains produced, on average, larger amounts of group B polysaccharide than did the 11 positive strains (reciprocal geometric mean titers, 676 and 224, respectively; $P < 0.05$), which suggests that the capsule may limit the accessibility of NspA surface epitopes. Given these strain differences in NspA surface accessibility, an rNspA-based meningococcal B vaccine may have to be supplemented by

additional antigens.

L125 ANSWER 7 OF 57 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 97258610 MEDLINE
DOCUMENT NUMBER: 97258610 PubMed ID: 9104804
TITLE: Highly conserved Neisseria meningitidis surface protein confers protection against experimental infection.
AUTHOR: Martin D; Cadieux N; Hamel J; Brodeur B R
CORPORATE SOURCE: Unite de Recherche en Vaccinologie, Centre de Recherche en Infectiologie, Centre Hospitalier Universitaire de Quebec, Ste-Foy, Canada.
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1997 Apr 7) 185 (7) 1173-83.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U52066
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970514

AB A new surface protein, named NspA, which is distinct from the previously described Neisseria meningitidis outer membrane proteins was identified. An NspA-specific mAb, named Me-1, reacted with 99% of the meningococcal strains tested indicating that the epitope recognized by this particular mAb is widely distributed and highly conserved. Western immunoblotting experiments indicated that mAb Me-1 is directed against a protein band with an approximate molecular mass of 22,000, but also recognized a minor protein band with an approximate molecular mass of 18,000. This mAb exhibited bactericidal activity against four meningococcal strains, two isolates of serogroup B, and one isolate from each serogroup A and C, and passively protected mice against an experimental infection. To further characterize the NspA protein and to evaluate the protective potential of recombinant NspA protein, the nspA gene was identified and cloned into a low copy expression vector. Nucleotide sequencing of the meningococcal insert revealed an ORF of 525 nucleotides coding for a polypeptide of 174 amino acid residues, with a predicted molecular weight of 18,404 and a isoelectric point of 9.93. Three injections of either 10 or 20 microg of the affinity-purified recombinant NspA protein efficiently protected 80% of the mice against a meningococcal deadly challenge comparatively to the 20% observed in the control groups. The fact that the NspA protein can elicit the production of bactericidal and protective antibodies emphasize its potential as a vaccine candidate.

L125 ANSWER 8 OF 57 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 94078651 MEDLINE
DOCUMENT NUMBER: 94078651 PubMed ID: 8256502
TITLE: **Transferrin-binding** proteins isolated from Neisseria meningitidis elicit protective and bactericidal antibodies in laboratory animals.
AUTHOR: Danve B; Lissolo L; Mignon M; Dumas P; Colombani S; Schryvers A B; Quentin-Millet M J
CORPORATE SOURCE: Pasteur Merieux Serums et Vaccins, Marcy l'Etoile, France.
SOURCE: VACCINE, (1993 Sep) 11 (12) 1214-20.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940203
Last Updated on STN: 20021218
Entered Medline: 19940112

AB **Transferrin-binding** proteins (Tbps) were affinity-isolated from group B Neisseria meningitidis strain B16B6 and used to raise specific antisera. Administration of the antisera to mice loaded with human transferrin before bacterial challenge significantly protected the animals from death. In active immunization studies, mice received three 25 micrograms injections of purified Tbps over a period of 28 days, 7 days after which they were challenged with N. meningitidis. The survival rate in immunized mice was much higher than in control groups. In both active and passive immunization experiments mice were protected against at least 100 LD50. A specific Tbp antiserum was highly bactericidal against the parent strain and against approximately half of the strains tested.

L125 ANSWER 9 OF 57 MEDLINE
ACCESSION NUMBER: 2002475314 MEDLINE
DOCUMENT NUMBER: 22222420 PubMed ID: 12236996
TITLE: [Influence of adjuvants on the ability of anti-Tbp antibodies to block **transferrin binding**, iron uptake and growth of Neisseria meningitis]. Influencia de adyuvantes en la capacidad de los anticuerpos anti-Tbps de bloquear la union de transferrina, la asimilacion de hierro y el crecimiento en Neisseria meningitidis.
COMMENT: Comment in: Enferm Infecc Microbiol Clin. 2002 Aug-Sep;20(7):313-5
AUTHOR: Ferreiros Carlos; Ferreiro Nuria; Criado M T
CORPORATE SOURCE: Departamento de Microbiologia, Facultad de Farmacia, Universidad de Santiago de Compostela, La Coruna, Espana.
SOURCE: ENFERMEDADES INFECCIOSAS Y MICROBIOLOGIA CLINICA, (2002 Aug-Sep) 20 (7) 316-20.
Journal code: 9104081. ISSN: 0213-005X.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20020919
Last Updated on STN: 20021217
Entered Medline: 20021210

AB OBJECTIVE: To evaluate the effect of five adjuvants on the ability of specific anti-TbpA/B to block iron uptake in Neisseria meningitidis. MATERIALS AND METHODS: **Transferrin binding** complexes (TbpA/B) purified from a TbpB isotype II Neisseria meningitidis strain were used to obtain sera with five different adjuvant formulations in mice in order to test the effect of the adjuvant on the ability of specific anti-TbpA/B antibodies to block **transferrin binding**, iron uptake and growth by meningococci. RESULTS: Levels of anti-TbpA/B antibodies were relatively low (1:125 in most cases), the highest being obtained with the RAS adjuvant (1:3125). Despite the relatively low responses, all sera were able to significantly inhibit **transferrin binding**, iron uptake and growth in the homologous strain. Nevertheless, the effect on a strain with a TbpB isotype different from that of the immunizing strain was almost nil, a result in keeping with the described division of the meningococci into at least two TbpB groups (isotypes I and II). CONCLUSIONS: In contrast to previous results for another important meningococcal protein, FbpA, the use of various adjuvants in the immunization of mice with TbpA/B complexes did not

produce differences in the immune responses elicited, except in relation to antibody titers.

L125 ANSWER 10 OF 57 MEDLINE
ACCESSION NUMBER: 2000428040 MEDLINE
DOCUMENT NUMBER: 20407297 PubMed ID: 10948108
TITLE: Allelic diversity of the two **transferrin binding** protein B gene isotypes among a collection of Neisseria meningitidis strains representative of serogroup B disease: implication for the composition of a recombinant TbpB-based vaccine.
AUTHOR: Rokbi B; Renauld-Mongenie G; Mignon M; Danve B; Poncet D; Chabanel C; Caugant D A; Quentin-Millet M J
CORPORATE SOURCE: Aventis Pasteur, Marcy-L'Etoile, France.. Bachra.Rokbi@aventis.com
SOURCE: INFECTION AND IMMUNITY, (2000 Sep) 68 (9) 4938-47. Journal code: 0246127.. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20021218
Entered Medline: 20000908

AB The distribution of the two isotypes of tbpB in a collection of 108 serogroup B meningococcal strains belonging to the four major clonal groups associated with epidemic and hyperendemic disease (the ET-37 complex, the ET-5 complex, lineage III, and cluster A4) was determined. Isotype I strains (with a 1.8-kb tbpB gene) was less represented than isotype II strains (19.4 versus 80.6%). Isotype I was restricted to the ET-37 complex strains, while isotype II was found in all four clonal complexes. The extent of the allelic diversity of tbpB in these two groups was studied by PCR restriction analysis and sequencing of 10 new tbpB genes. Four major tbpB gene variants were characterized: B16B6 (representative of isotype I) and M982, BZ83, and 8680 (representative of isotype II). The relevance of these variants was assessed at the antigenic level by the determination of cross-bactericidal activity of purified immunoglobulin G preparations raised to the corresponding recombinant TbpB (rTbpB) protein against a panel of 27 strains (5 of isotype I and 22 of isotype II). The results indicated that rTbpB corresponding to each variant was able to induce cross-bactericidal antibodies. However, the number of strains killed with an anti-rTbpB serum was slightly lower than that obtained with an anti-TbpA(+)B complex. None of the sera tested raised against an isotype I strain was able to kill an isotype II strain and vice versa. None of the specific antisera tested (anti-rTbpB or anti-TbpA(+)B complex) was able to kill all of the 22 isotype II strains tested. Moreover, using sera raised against the C-terminus domain of TbpB M982 (amino acids 352 to 691) or BZ83 (amino acids 329 to 669) fused to the maltose-binding protein, cross-bactericidal activity was detected against 12 and 7 isotype II strains, respectively, of the 22 tested. These results suggest surface accessibility of the C-terminal end of TbpB. Altogether, these results show that although more than one rTbpB will be required in the composition of a TbpB-based vaccine to achieve a fully cross-bactericidal activity, rTbpB and its C terminus were able by themselves to induce cross-bactericidal antibodies.

L125 ANSWER 11 OF 57 MEDLINE
ACCESSION NUMBER: 1998379566 MEDLINE
DOCUMENT NUMBER: 98379566 PubMed ID: 9713939
TITLE: Effect of adjuvants in the isotypes and bactericidal

activity of antibodies against the **transferrin-binding** proteins of Neisseria meningitidis.
AUTHOR: Gomez J A; Hernandez E; Criado M T; Ferreiros C M
CORPORATE SOURCE: Departamento de Microbiologia y Parasitologia, Facultad de Farmacia, Universidad de Santiago de Compostela, Spain.
SOURCE: VACCINE, (1998 Oct) 16 (17) 1633-9.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 20021218
Entered Medline: 19981022

AB Twenty-eight Neisseria meningitidis strains of different serogroups, serotypes, and TbpB isotypes were used to test the effect of five adjuvant formulations on the immune response to the meningococcal **transferrin-binding** proteins (Tbps) in mice. Levels of anti-Tbps antibodies were relatively low when purified TbpA-TbpB complexes were used for immunization, those obtained with the RAS adjuvant being the highest, and the isotype distribution reveals a prevalence of the non-bactericidal IgG1. Specific anti-Tbps antibody levels were five to 125 times higher immunizing with whole outer membrane vesicles, with bactericidal isotypes prevailing, which suggests that presentation of these antigens in their natural conformation is crucial to elicit a good response. Nevertheless, bactericidal activity did not correlate with these characteristics, confirming that it must be also influenced by other factors, and direct evaluation of the killing ability is necessary to draw conclusions about the efficacy of antigens or adjuvants in vaccine design.

L125 ANSWER 12 OF 57 MEDLINE
ACCESSION NUMBER: 97130016 MEDLINE
DOCUMENT NUMBER: 97130016 PubMed ID: 8975892
TITLE: Evaluation of recombinant **transferrin-binding** protein B variants from Neisseria meningitidis for their ability to induce cross-reactive and bactericidal antibodies against a genetically diverse collection of serogroup B strains.
AUTHOR: Rokbi B; Mignon M; Maitre-Wilmotte G; Lissolo L; Danve B; Caugant D A; Quentin-Millet M J
CORPORATE SOURCE: Pasteur Merieux Serums et Vaccins, Marcy-l'Etoile, France.
SOURCE: INFECTION AND IMMUNITY, (1997 Jan) 65 (1) 55-63.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 20021218
Entered Medline: 19970203

AB **Transferrin-binding** protein B (TbpB) is a surface-exposed protein, variable among strains of Neisseria meningitidis, that has been considered as a vaccine candidate. To define a TbpB molecule that would give rise to broadly cross-reactive antibodies with TbpB of many strains, specific antisera were produced against three recombinant TbpB variants from strain M982: one corresponding to the full-length TbpB; one in which stretches of amino acids located in the central part of the molecule, described as hypervariable, have been deleted; and one corresponding to the N-terminal half of the molecule,

described as the human **transferrin binding** domain.
The reactivity of these antisera against 58 serogroup B strains with a 2.1-kb tbpB gene representing different genotypes, serotypes, and subtypes and different geographic origins was tested on intact meningococcal cells. In parallel, the bactericidal activity of the antisera was evaluated against 15 of the 58 strains studied. Of the 58 strains, 56 (98%) reacted with the antiserum specific for the N-terminal half of TbpB M982; this antiserum was bactericidal against 9 of 15 strains (60%). On the other hand, 43 of 58 strains reacted with the antiserum raised to full-length TbpB while 12 of 15 (80%) were killed with this antiserum. The antiserum specific to TbpB deleted of its central domain gave intermediate results, with 53 of 58 strains (91.3%) recognized and 10 of 15 (66.6%) killed. These results indicate that the N-terminal half of TbpB was sufficient to induce cross-reactive antibodies reacting with the protein on meningococcal cells but that the presence of the C-terminal half of the protein is necessary for the induction of cross-bactericidal antibodies.

L125 ANSWER 13 OF 57 MEDLINE
ACCESSION NUMBER: 96198479 MEDLINE
DOCUMENT NUMBER: 96198479 PubMed ID: 8606350
TITLE: Transferrin receptors of Neisseria meningitidis: promising candidates for a broadly cross-protective vaccine.
AUTHOR: Ala'Aldeen D A
CORPORATE SOURCE: Division of Microbiology, Department of Clinical Laboratory Sciences, University Hospital, Queen's Medical Centre, Nottingham, UK.
SOURCE: JOURNAL OF MEDICAL MICROBIOLOGY, (1996 Apr) 44 (4) 237-43.
Ref: 40
Journal code: 0224131. ISSN: 0022-2615.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960531
Last Updated on STN: 20021218
Entered Medline: 19960523

AB Production of a meningococcal vaccine capable of generating long-lasting immunity in all age groups is still a high priority worldwide. Iron-regulated outer-membrane proteins have attracted considerable attention in recent years and it has become increasingly evident that the meningococcal **transferrin-binding** proteins, TBP1 and TBP2, have characteristics compatible with a safe and broadly cross-reactive vaccine candidate. Both TBPs are surface-exposed and immunogenic in man and animals, and antibodies to their native structure are bactericidal to homologous and many heterologous strains. These include strains from various serogroups, serotypes and serosubtypes, with no obvious correlation between bactericidal activity and the identity of the strains or the molecular mass of the heterogeneous TBP2 molecule. A meningococcal vaccine based on, or enriched with, undenatured TBPs from one or more strains, in combination with conventional polysaccharide-based vaccines, might increase the spectrum of strains against which protection can be achieved to include serogroup B strains. In this review, the structure-function and immunological properties of TBP1 and TBP2 are discussed.

L125 ANSWER 14 OF 57 MEDLINE
ACCESSION NUMBER: 96118129 MEDLINE
DOCUMENT NUMBER: 96118129 PubMed ID: 8578805

TITLE: Human antibody response to meningococcal **transferrin binding** proteins: evidence for vaccine potential.
AUTHOR: Gorringe A R; Borrow R; Fox A J; Robinson A
CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down, Salisbury, UK.
SOURCE: VACCINE, (1995 Sep) 13 (13) 1207-12.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960321
Last Updated on STN: 20021218
Entered Medline: 19960308

AB During iron-limited growth Neisseria meningitidis expresses two **transferrin binding** proteins, TBP1 and TBP2, with molecular masses of approximately 98 and 65-90 kDa depending on strain. Mixtures of TBP1 and TBP2 (TBP1 + 2) from three meningococcal strains were purified using affinity chromatography and used to determine anti-TBP antibodies in human sera by ELISA. Sera were obtained from healthy individuals, asymptomatic carriers of N. meningitidis and cases of meningococcal disease. Healthy individuals had little detectable antibody to TBPs but sera from carriers and cases exhibited a response demonstrating that TBPs are expressed in vivo during both carriage and disease. The ELISA absorbances produced by each of the individual sera to TBPs from the three meningococcal strains were compared and very high correlation coefficients were obtained, indicating that human anti-TBP antibodies, in contrast to mouse and rabbit antibodies, are cross-reactive between strains. Antibodies to separately purified TBP1 and TBP2 were also detected in both cases and carriers. The IgG and IgM response to TBP1 + 2 was greater in cases than carriers but the mean IgA response was the same. This demonstration of an antibody response that is cross-reactive between TBP types greatly strengthens the case for inclusion of TBPs in a meningococcal vaccine to protect against all serogroups and serotypes.

L125 ANSWER 15 OF 57 MEDLINE
ACCESSION NUMBER: 95172736 MEDLINE
DOCUMENT NUMBER: 95172736 PubMed ID: 7868259
TITLE: Evaluation of **transferrin-binding** protein 2 within the **transferrin-binding** protein complex as a potential antigen for future meningococcal vaccines.
AUTHOR: Lissolo L; Maitre-Wilmotte G; Dumas P; Mignon M; Danve B; Quentin-Millet M J
CORPORATE SOURCE: Pasteur Merieux Serums et Vaccins, Marcy l'Etoile, France.
SOURCE: INFECTION AND IMMUNITY, (1995 Mar) 63 (3) 884-90.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950407
Last Updated on STN: 20021218
Entered Medline: 19950330

AB Because the meningococcal transferrin receptor was shown to elicit bactericidal and protective antibodies in laboratory animals, we undertook a study of the protective role of each of the polypeptides within the

Tbp1-Tbp2 complex. We developed a procedure to purify from Neisseria meningitidis B16B6 the two proteins in milligram amounts and raised specific antisera in rabbits and mice. Only antisera specific for Tbp2 displayed bactericidal activity against the parent strain. Mice immunized with purified Tbp2 survived a lethal challenge to a similar degree as animals immunized with the Tbp1-Tbp2 complex, demonstrating that Tbp2 played an important role in the protective activity observed with the complex. Both Tbp1- and Tbp2-specific antisera inhibited **transferrin binding** to the purified receptor in a solid-phase binding assay, suggesting that the antibodies were able to interact with the Tbp1 molecule only when it was removed from its membrane environment. Finally, Tbp2-specific immunoglobulins were able to lower the growth rate of the meningococci when human transferrin was their sole iron source. Therefore, in all four different systems tested, Tbp2 or antibodies specific for Tbp2 displayed biological characteristics close to those of the Tbp1-Tbp2 complex. This suggests that Tbp2 plays an important role in the protective activity of the complex, eliciting antibodies that are not only bactericidal but also inhibitory for meningococcal growth.

L125 ANSWER 16 OF 57 MEDLINE
ACCESSION NUMBER: 94274318 MEDLINE
DOCUMENT NUMBER: 94274318 PubMed ID: 8005685
TITLE: Immune responses in humans and animals to meningococcal **transferrin-binding** proteins: implications for vaccine design.
AUTHOR: Ala'Aldeen D A; Stevenson P; Griffiths E; Gorringe A R; Irons L I; Robinson A; Hyde S; Borriello S P
CORPORATE SOURCE: Department of Microbiology, Queen's Medical Centre, Nottingham, United Kingdom.
SOURCE: INFECTION AND IMMUNITY, (1994 Jul) 62 (7) 2984-900. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940729
Last Updated on STN: 20021218
Entered Medline: 19940720

AB The results reported here show that the two meningococcal **transferrin-binding** proteins (TBP1 and TBP2) generate different immune responses in different host species and that there is variation in response dependent on the method of antigen preparation and possibly the route of administration. Mice immunized with either whole cells of Neisseria meningitidis SD (B:15:P1.16) or the isolated TBP1-TBP2 complex from the same strain produced antisera which, when tested against a representative panel of meningococcal isolates by Western blotting (immunoblotting), recognized some but not all heterologous TBP2 molecules. In contrast, rabbit antisera raised to the same preparations were cross-reactive with almost all the TBP2 molecules. The immune response to TBP1 was also host species dependent. Western blot analysis with denatured TBP1 failed to detect antibodies in antisera raised in mice to whole cells or in a rabbit to the TBP1-TBP2 complex but detected broadly cross-reactive antibodies in mouse anti-TBP1-TBP2 complex sera and strain-specific antibodies in rabbit anti-whole-cell serum. Human convalescent-phase sera obtained from five patients infected with meningococci of different serogroups and serotypes contained fully cross-reactive antibodies to TBP2 but no anti-TBP1 antibodies, when examined on Western blots. However, on dot immunoblots, the same patients' sera, as well as the mouse anti-whole cell and the rabbit

anti-TBP1-TBP2 complex sera, reacted with purified biologically active TBP1 of strain SD. This indicates that native TBP1, a protein which loses its biological and some of its immunological activities when denatured, is immunogenic and that humans generate cross-reactive antibodies to native epitopes. These observations have important implications for assessing the vaccine potential of TBPs and other meningococcal antigens. Conclusions regarding the usefulness of TBPs as candidate components of meningococcal serogroup B vaccines based on results from certain animal species such as mice, or on methods such as Western blotting, may have little bearing on the situation in humans and may lead to some potentially useful antigens being disregarded.

L125 ANSWER 17 OF 57 MEDLINE
ACCESSION NUMBER: 90354049 MEDLINE
DOCUMENT NUMBER: 90354049 PubMed ID: 2117572
TITLE: Expression of Neisseria meningitidis iron-regulated outer membrane proteins, including a 70-kilodalton transferrin receptor, and their potential for use as vaccines.
AUTHOR: Banerjee-Bhatnagar N; Frasch C E
CORPORATE SOURCE: Center for Biologics Evaluation and Research, Division of Bacterial Products, Bethesda, Maryland 20892.
SOURCE: INFECTION AND IMMUNITY, (1990 Sep) 58 (9) 2875-81. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 19901026
Last Updated on STN: 19970203
Entered Medline: 19900927

AB The iron-regulated proteins (IRPs) of five group B meningococcal strains expressing class 2 outer membrane proteins were compared with those of five strains expressing class 3 proteins. Three to four high-molecular-weight IRPs were expressed by each strain, but their molecular sizes varied between strains and were not related to class 2 or 3 protein expression. Transferrin and hemoglobin could be used as a sole iron source. By using anti-human transferrin antibodies, it was shown that meningococcal cells and purified outer membranes bound transferrin. Growth under conditions of iron limitation caused a several-fold increase in the amount of transferrin bound to the cell surface. The **transferrin-binding** protein was detergent solubilized from outer membranes and partially purified. The isolated protein bound human transferrin and had an apparent molecular mass of 70 kilodaltons. To evaluate the potential of vaccines containing IRPs, we prepared outer membrane vaccines from strains M986-NCV-1 (M986) (--:2a: P1.2) and 44/76-M25 (44/76) (--:15:P1.15) grown to fully express their IRPs. Both vaccines induced significant anti-IRP antibodies as measured by enzyme immunoassay and by Western immunoblot with both M986 and 44/76 outer membranes. By Western blot analysis, the M986 vaccine induced antibodies to two different IRPs, one of which was shared with 44/76. Since the IRPs are major in vivo-expressed outer membrane proteins and are required for survival in vivo, these proteins should be evaluated for their usefulness in a group B meningococcal vaccine.

L125 ANSWER 18 OF 57 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
ACCESSION NUMBER: 2000:608607 CAPLUS
DOCUMENT NUMBER: 133:213155
TITLE: Neisserial vaccine compositions and methods
INVENTOR(S): Robinson, Andrew; Gorringe, Andrew Richard; Hudson, Michael John; Bracegirdle, Philippa; Kroll, John

Simon; Cartwright, Keith
PATENT ASSIGNEE(S): Microbiological Research Authority, UK; Imperial College School of Science, Technology and Medicine; Public Health Laboratory Service Board
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050074	A2	20000831	WO 2000-GB624	20000222
WO 2000050074	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1154791	A2	20011121	EP 2000-905182	20000222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537352	T2	20021105	JP 2000-600684	20000222
US 2003026809	A1	20030206	US 2001-942583	20010831
US 2003021812	A1	20030130	US 2002-185769	20020701

PRIORITY APPLN. INFO.:

GB 1999-4028	A	19990222
GB 1999-22561	A	19990923
WO 2000-GB624	W	20000222
US 2001-914041	A1	20010822

AB Methods and compns. for the treatment of microbial infection, and in particular meningococcal disease, comprise a commensal Neisseria or an ext. of a commensal Neisseria. Further methods and compns. comprise commensal Neisseria which express genes from virulent strains of Neisseria and/or heterologous gene products from non-neisserial sources. Such compns. are used in vaccine prepns. for the treatment of microbial infection.

L125 ANSWER 19 OF 57 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 8
ACCESSION NUMBER: 1999:554625 CAPLUS
DOCUMENT NUMBER: 131:298445
TITLE: Bactericidal and cross-protective activities of a monoclonal antibody directed against Neisseria meningitidis **NspA** outer membrane protein
AUTHOR(S): Cadieux, Nathalie; Plante, Martin; Rioux, Clement R.; Hamel, Josee; Brodeur, Bernard R.; Martin, Denis
CORPORATE SOURCE: Unite de Recherche en Vaccinologie, Centre Hospitalier Universitaire de Quebec et Universite Laval, Ste-Foy, QC, G1V 4G2, Can.
SOURCE: Infection and Immunity (1999), 67(9), 4955-4959
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cross-bactericidal and cross-protective activities of a monoclonal antibody (MAb) named Me-7, which is directed against an antigenically highly conserved epitope on the meningococcal **NspA** protein, were

studied. This MAb efficiently killed in vitro, in the presence of rabbit or human serum, 13 of 14 meningococcal strains tested, including 9 of 9, 2 of 3, and 2 of 2 strains of serotypes B, A, and C, resp. MAb Me-7 also significantly reduced by more than 75% the levels of bacteremia recorded for mice challenged with 10 of 11 meningococcal strains tested. Anal. of the predicted amino acid sequence of the **NspA** protein from the meningococcal strain MCH88 (A:4:P1.10), which was not killed by MAb Me-7, indicated the presence of an addnl. glutamine residue at position 73, compared to the three other **NspA** sequences. The data presented in this study suggest that antibodies directed against this highly conserved outer membrane protein could protect against meningococcal infections.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L125 ANSWER 20 OF 57 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 10
ACCESSION NUMBER: 1994:453819 CAPLUS
DOCUMENT NUMBER: 121:53819
TITLE: Cloning and expression of genes for the subunits of the **transferrin** receptor of Neisseria meningitidis
INVENTOR(S): Jacobs, Eric; Legrain, Michele; Mazarin, Veronique; Bouchon-Theisen, Bernadette; Shryvers, Anthony B.; Bloch, Marie Aline
PATENT ASSIGNEE(S): Pasteur Merieux Serums et Vaccins S.A., Fr.; Transgene SA
SOURCE: Fr. Demande, 61 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2692592	A1	19931224	FR 1992-7493	19920619
FR 2692592	B1	19950331		
AU 9340098	A1	19931223	AU 1993-40098	19930608
AU 679911	B2	19970717		
CA 2098448	AA	19931220	CA 1993-2098448	19930615
EP 586266	A1	19940309	EP 1993-401531	19930615
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9302222	A	19931220	NO 1993-2222	19930616
HU 68443	A2	19950628	HU 1993-1791	19930618
HU 219267	B	20010328		
JP 06277066	A2	19941004	JP 1993-173773	19930621
US 6028049	A	20000222	US 1995-448194	19950523
US 6326350	B1	20011204	US 1997-867921	19970603

PRIORITY APPLN. INFO.:
FR 1992-7493 A 19920619
US 1993-78053 B1 19930618
US 1994-361469 A1 19941222
US 1995-445472 B1 19950522

AB Genes for the subunits of the Neisseria meningitidis **transferrin** receptors of a group of isolates are cloned for expression for manuf. of the proteins. The proteins are exposed on the bacterial surface and so are potential antigens for for vaccines. The receptor was purified from bacterial lysates by binding with biotinylated **transferrin**, followed by solubilization with Sarkosyl/EDTA and affinity purifn. of the complex with streptavidin agarose. The purified protein was used to raise antiserum to the receptor and N-terminal peptide sequences detd. A randomly fragmented **N. meningitidis** bank in

.lambda.ZAP was screened with the antiserum and two independent clones obtained and further rounds of screening was conducted to ensure that full-length clones were obtained. The 5'-ends of the coding sequences were located using the N-terminal peptide sequences. Manuf. of the subunits in Escherichia coli using the pelB leader peptide of Erwinia carotovora to direct secretion is demonstrated.

L125 ANSWER 21 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:277876 CAPLUS
DOCUMENT NUMBER: 132:313678
TITLE: Metal salt particle-adsorbed adjuvant systems and vaccines
INVENTOR(S): Garcon, Nathalie
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S. A., Belg.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023105	A2	20000427	WO 1999-EP7764	19991008
WO 2000023105	A3	20000803		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9915545	A	20010814	BR 1999-15545	19991008
EP 1126876	A2	20010829	EP 1999-970607	19991008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 750587	B2	20020725	AU 2000-11518	19991008
NZ 511113	A	20020927	NZ 1999-511113	19991008
NO 2001001801	A	20010530	NO 2001-1801	20010409
ZA 2001002954	A	20020520	ZA 2001-2954	20010410

PRIORITY APPLN. INFO.:

GB 1998-22703	A	19981016
GB 1998-22709	A	19981016
GB 1998-22712	A	19981016
WO 1999-EP7764	W	19991008

AB The present invention provides vaccine and adjuvant formulations comprising an immunostimulant and a metal salt. The immunostimulant is adsorbed onto a particle of metal salt (e.g. aluminum hydroxide or phosphate) and the resulting particle is essentially devoid of antigen.

L125 ANSWER 22 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:469887 CAPLUS
DOCUMENT NUMBER: 133:221322
TITLE: Bactericidal antibody response to Neisseria meningitidis serogroup B in patients with bacterial meningitis: effect of immunization with an outer membrane protein vaccine
AUTHOR(S): Milagres, L. G.; Gorla, M. C. O.; Rebelo, M. C.; Barroso, D. E.
CORPORATE SOURCE: Bacteriology Section, Adolfo Lutz Institute, Sao

Paulo, Brazil
SOURCE: FEMS Immunology and Medical Microbiology (2000), 28(4), 319-327
CODEN: FIMIEV; ISSN: 0928-8244
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors evaluated the bactericidal antibody response to Neisseria meningitidis serogroup B in convalescent patients from bacterial meningitis. Patients infected with B meningococci were stratified according to their vaccination status (Cuban BC vaccine) into group 1 (immunized) and group 2 (non-immunized). The results suggested that antibody titers .gtoreq.2 (log2) indicate a specific immune response to **N. meningitidis**. In group 1, 64% of patients had a significant antibody titer (.gtoreq.2) in their acute sera against a B:4:P1.15 strain, compared to only 21% of group 2 patients. All patients from group 1 without bactericidal antibodies in their acute sera had a significant increase (at least 2-fold increase in log2 titers) in antibody titers in their convalescent sera, in contrast, to only 27% of patients from group 2. Using mutant strains lacking OMP1 or OMP5, it was shown that OMP1 was an important antigen recognized by immunized patients but not by non-immunized patients.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L125 ANSWER 23 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:746464 CAPLUS
DOCUMENT NUMBER: 132:77240
TITLE: Molecular mimetics of polysaccharide epitopes as vaccine candidates for prevention of Neisseria meningitidis serogroup B disease
AUTHOR(S): Moe, G. R.; Tan, S.; Granoff, D. M.
CORPORATE SOURCE: Children's Hospital Oakland Research Institute, Oakland, CA, USA
SOURCE: FEMS Immunology and Medical Microbiology (1999), 26(3-4), 209-226
CODEN: FIMIEV; ISSN: 0928-8244
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 121 refs. Neisseria meningitidis is a major cause of meningitis and sepsis. Despite nearly 25 yr of work, there is no promising vaccine candidate for prevention of disease caused by meningococcal B strains. This review summarizes newer approaches for eliciting protective meningococcal B immune responses, including the use of mol. mimetics of group B polysaccharide and conserved membrane proteins as immunogens. The capsular polysaccharide of this organism is conserved and serum antibody to this capsule confers protection against disease. However, the immunogenicity of meningococcal B polysaccharide-based vaccines is poor. Further, a portion of the antibody elicited has autoantibody activity. Recently, the authors' lab. produced a panel of murine monoclonal antibodies (Mabs) that react specifically with capsular polysaccharide epitopes on meningococcal B that are distinct from host polysialic acid. These Mabs elicit complement-mediated bactericidal activity and confer passive protection in animal models. The anti-capsular Mabs were used to identify mol. mimetics from phage display peptide libraries. The resulting peptides were antigenic mimetics as defined by binding to the Mabs used to select them but, to date, are poor immunogenic mimetics in failing to elicit anti-capsular antibodies.
REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L125 ANSWER 24 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:71228 CAPLUS
DOCUMENT NUMBER: 128:164910
TITLE: Genes and gene products specific to pathogenicity of Neisseria meningitidis, methods for obtaining them and their biological applications
INVENTOR(S): Nassif, Xavier; Tinsley, Colin; Achtman, Mark; Ruelle, Jean-Louis; Vinals, Carla; Merker, Petra
PATENT ASSIGNEE(S): Institut National De La Sante Et De La Recherche Medicale (INSERM), Fr.; Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V., Berlin; Smithkline Beecham; Nassif, Xavier; Tinsley, Colin; Achtman, Mark; Ruelle, Jean-Louis; Vinals, Carla; Merker, Petra
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9802547	A2	19980122	WO 1997-FR1295	19970711
WO 9802547	A3	19980409		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2751000	A1	19980116	FR 1996-8768	19960712
FR 2751000	B1	19981030		
AU 9736977	A1	19980209	AU 1997-36977	19970711
AU 730423	B2	20010308		
EP 951552	A2	19991027	EP 1997-933727	19970711
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001504684	T2	20010410	JP 1998-505685	19970711
US 2002164603	A1	20021107	US 2001-928457	20010814

PRIORITY APPLN. INFO.:
FR 1996-8768 A 19960712
WO 1997-FR1295 W 19970711
US 1999-214759 B1 19990422

AB DNA sequences that are found in Neisseria meningitidis that are unique to it, specific to pathogenesis, and not found in N. gonorrhoeae, **N. lactamica** or **N. cinerea** are cloned by representational difference anal. A no. of genes assocd. with pathogenesis that are found in **N. meningitidis** and N.gonorrhoeae including the genes of biosynthesis of the polysaccharide capsule (frpA, frpC, porA), pilC, the genes for rotamase, IgA protease, pilin, transferring-binding proteins and opacity proteins and the sequence IS1106. The genes map in clusters in three regions of the chromosome. The gene products can be used as antigens in the raising of antibodies for diagnostic or therapeutic uses, e.g. specific immunoassays or vaccines. The roles of the genes in pathogenesis can be studied by targeted deletion.

L125 ANSWER 25 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:97206 CAPLUS

DOCUMENT NUMBER: 128:203874
TITLE: Meningococcal vaccine development: a novel approach
AUTHOR(S): Fusco, Peter C.; Blake, M. S.; Michon, Francis
CORPORATE SOURCE: North American Vaccine, Inc., Beltsville, MD, 20705, USA
SOURCE: Expert Opinion on Investigational Drugs (1998), 7(2), 245-252
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neisseria meningitidis is a major world-wide cause of meningitis. Effective capsular polysaccharide (CPS) vaccines, that elicit CPS-specific bactericidal (BC) antibodies, were previously developed and licensed to protect against meningococcal disease. However, due to their T-cell independent character, CPS vaccines are useless in infants and do not provide immunol. memory or long-lasting protection in adults. CPS-protein conjugate vaccines are being developed to improve and broaden vaccine efficacy by creating T-cell dependent antigens. However, group B meningococci (GBM) are responsible for nearly half of meningococcal disease and possess a CPS, composed of polysialic acid, that is poorly immunogenic. N-propionyl (NPr) modification of the GBM polysaccharide (GBMP) has enhanced its immunogenicity, but BC antibodies are not induced at high levels, even when conjugated to conventional protein carriers, unless adjuvants stronger than aluminum hydroxide are used. We have chosen to couple the NPr-GBMP by reductive amination to a recombinant GBM class 3 porin (rProB), which we have shown to modulate the immune response in animals towards the prodn. of CPS-specific BC antibodies. We have also combined this conjugate with similar CPS-rProB conjugates for groups A and C meningococci to form a trivalent A/B/C conjugate vaccine. This trivalent meningococcal vaccine has been shown to be safe and highly immunogenic in mice and non human primates, generating CPS-specific BC antibodies for each of the 3 major serogroups, which should provide world-wide protection against meningococcal disease.

L125 ANSWER 26 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:682985 CAPLUS
DOCUMENT NUMBER: 127:355819
TITLE: Heterogeneity of tbpB, the **transferrin** -binding protein B gene, among serogroup B Neisseria meningitidis strains of the ET-5 complex
AUTHOR(S): Rokbi, B.; Mignon, M.; Caugant, D. A.; Quentin-Millet, M. J.
CORPORATE SOURCE: Pasteur Merieux Connaught, Marcy-l'Etoile, Fr.
SOURCE: Clinical and Diagnostic Laboratory Immunology (1997), 4(5), 522-529
CODEN: CDIMEN; ISSN: 1071-412X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB ET-5 complex strains of Neisseria meningitidis were traced intercontinentally and have been causing hyperendemic meningitis on a worldwide scale. In an attempt to develop a fully broad cross-reactive **transferrin**-binding protein B (TbpB)-based vaccine, we undertook to assess the extent of variability of TbpB proteins among strains of this epidemiol. complex. For this purpose, a PCR-based method was developed to study the heterogeneity of the tbpB genes from 31 serogroup B **N. meningitidis** strains belonging to the ET-5 complex. To define adequate primers, the tbpB gene from an ET-5 complex strain, 8680 (B:15:P13; isolated in Chile in 1987), was cloned and the nucleotide sequence was detd. and compared to two other previously published tbpB

sequences. A tbpB fragment was amplified from genomic DNA from each of the 31 strains. By this method, heterogeneity in size was obsd. and further characterized by restriction pattern anal. with four restriction enzymes and by sequencing tbpB genes from three other ET-5 complex strains. Four distinct tbpB gene types were identified. Fifty-five percent of the strains studied (17/31) harbored tbpB genes similar to that of strain BZ83 (B:15:-) isolated in The Netherlands in 1984. Ten of the 31 strains (32.2%) had tbpB genes close to that of strain M982. Only 3 of the 31 (9.6%) were found to harbor tbpB genes close to that of strain 8680, and finally one strain, 8710 (B:15:P1.3; isolated in Chile in 1987), was found to harbor a tbpB gene different from all the others. These results demonstrated a pronounced variability among tbpB alleles within a limit- ed no. of ET-5 complex strains collected over a 19-yr period. Despite the genetic heterogeneity obsd., specific antisera raised to purified Tbps from ET-5 complex strains showed broad cross-reactivity between different TbpBs both by Western blot anal. and bactericidal assay, confirming that a limited no. of TbpB mols. included in a vaccine are likely to induce broadly cross-reactive antibodies against the different strains.

L125 ANSWER 27 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:679407 CAPLUS
DOCUMENT NUMBER: 127:357830
TITLE: Analysis of the human Ig isotype response to individual **transferrin** binding proteins A and B from Neisseria meningitidis
AUTHOR(S): Johnson, Alison S.; Gorringe, Andrew R.; Fox, Andrew J.; Borrow, Ray; Robinson, Andrew
CORPORATE SOURCE: Manchester Public Health Laboratory, Withington Hospital, Manchester, M20 2LR, UK
SOURCE: FEMS Immunology and Medical Microbiology (1997), 19(2), 159-167
CODEN: FIMIEV; ISSN: 0928-8244
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Subcapsular antigens, including **transferrin** binding proteins, are being considered as potential vaccines against serogroup B meningococci. This study examd. the human isotype antibody responses in cases of meningococcal disease to meningococcal TbpA (**transferrin** binding protein A) and TbpB (**transferrin** binding protein B) from 2 strains (SD and B16B6) expressing high and low mol. mass TbpB resp. TbpA isolated from both strains were recognized more frequently and higher durable ELISA absorbance values were detected than those detected against TbpB from either strain. These antibody responses to Tbps were independent of the infecting meningococcal strain type. The antibody response to the 4 proteins was highly variable between individuals and differed against all 4 antigens. The variability of immune responses to each Tbp from the 2 strains suggests that a successful vaccine would need to include TbpA and TbpB from a no. of strains.

L125 ANSWER 28 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:608836 CAPLUS
DOCUMENT NUMBER: 117:208836
TITLE: **Transferrin**-binding proteins (TBPs) from Neisseria gonorrhoeae and Neisseria meningitidis
INVENTOR(S): Sparling, P. Frederick; Cornelissen, Cynthia Nau
PATENT ASSIGNEE(S): University of North Carolina, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9203467	A1	19920305	WO 1991-US6026	19910823
W: AU, CA, FI, HU, JP, KR, NO, RO, SU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2087958	AA	19920224	CA 1991-2087958	19910823
AU 9187477	A1	19920317	AU 1991-87477	19910823
EP 546118	A1	19930616	EP 1991-918802	19910823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06500562	T2	19940120	JP 1991-517184	19910823
JP 2002186489	A2	20020702	JP 2001-296757	19910823

PRIORITY APPLN. INFO.: US 1990-572187 A 19900823
JP 1991-517184 A3 19910823
WO 1991-US6026 A 19910823

AB Fe-regulated proteins in outer membranes of N. gonorrhoeae and **N**. **meningitidis** (mol. wts. 100 and 95 kDa, resp.), isolated with a **transferrin** affinity column, function as **transferrin** receptors. Antibodies to the Fe-regulated TBPs, and vaccines contg. the TBPs, are useful for treating and preventing Neisseria infections, resp. Methods for immunol. detection of the TBPs and their antibodies, and partial DNA sequences coding for the TBPs, are given. Thus, chromosomal DNA fragments from gonococcal strain FA19 were ligated into .lambda. gt11 DNA, cloned in Escherichia coli, and screened with antisera to TBP, and the identified DNA was amplified by PCR and sequenced.

L125 ANSWER 29 OF 57 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003096149 EMBASE
TITLE: Meningococcal vaccines.
AUTHOR: Collins C.L.; Pollard A.J.
CORPORATE SOURCE: C.L. Collins, Department of Paediatrics, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom. clare.collins@paediatrics.ox.ac.uk
SOURCE: Current Opinion in Investigational Drugs, (1 Jul 2002) 3/7 (975-979).
Refs: 44
ISSN: 1472-4472 CODEN: CIDREE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
003 Endocrinology
026 Immunology, Serology and Transplantation
030 Pharmacology
038 Adverse Reactions Titles
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Neisseria** meningitidis is one of the leading infectious causes of death in children under five years old in industrialized countries, and most cases can be attributed to five disease-causing serogroups: A, B, C, Y and W135. Meningococcal vaccine development began in the 1930s with killed whole-cell and exotoxin vaccines, but widespread use of polysaccharide vaccines did not begin until the 1970s. Serogroup A, C, Y and W135 polysaccharides are all included in vaccines for travellers, other high risk groups and control of outbreaks, but have limited immunogenicity and efficacy in childhood. Protein-polysaccharide conjugate vaccines overcome this problem and offer the possibility of protection in

early childhood from serogroup A, C, Y and W135. An effective serogroup B vaccine remains elusive and the greatest challenge for vaccine developers.

L125 ANSWER 30 OF 57 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002383915 EMBASE
TITLE: Challenges for the development of vaccines against Haemophilus influenzae and **Neisseria** meningitidis.
AUTHOR: Cripps A.W.; Foxwell R.; Kyd J.
CORPORATE SOURCE: A.W. Cripps, Gadi Res. Ctr. for Hlth./Med. Sci., University of Canberra, Canberra, ACT 2601, Australia. allan.cripps@canberra.edu.au
SOURCE: Current Opinion in Immunology, (1 Oct 2002) 14/5 (553-557). Refs: 33
ISSN: 0952-7915 CODEN: COPIEL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The development of protein-polysaccharide conjugate vaccines has had a major impact on Haemophilus influenzae type b disease. The application of this technology to **Neisseria** meningitidis is also striking, particularly for serogroup C. However, significant challenges exist for the development of vaccines against non-typeable H. influenzae and against N. meningitidis serogroup B. Issues such as non-vaccine-strain replacement and correlates of protection need to be addressed as well as the longer-term implications of vaccination against what are essentially 'normal' microflora.

L125 ANSWER 31 OF 57 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002187368 EMBASE
TITLE: Meningococcal disease: How to prevent and how to manage.
AUTHOR: Balmer P.; Miller E.
CORPORATE SOURCE: Dr. E. Miller, Immunisation Division, Public Health Laboratory Service, Communicable Dis. Surveillance Ctr., 61 Colindale Avenue, London NW9 5EQ, United Kingdom. emiller@phls.org.uk
SOURCE: Current Opinion in Infectious Diseases, (2002) 15/3 (275-281). Refs: 93
ISSN: 0951-7375 CODEN: COIDE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Meningococcal disease is a significant problem in the paediatric population. The diagnosis of meningococcal disease can be problematic and progression of the disease can rapidly lead to a life-threatening illness. Despite the success of antibiotic treatment, mortality rates remain high. The development of protein-polysaccharide conjugate vaccines has significantly improved the success of vaccination in reducing the incidence of meningococcal disease. However, a comprehensive vaccine conferring protection against disease-associated serogroups remains elusive. The aim of this review is to highlight recent significant improvements in the prevention and management of meningococcal disease.

L125 ANSWER 32 OF 57 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000325477 EMBASE
TITLE: Distribution of **Neisseria** meningitidis serogroup B serosubtypes and serotypes circulating in the United States.
AUTHOR: Tondella M.L.C.; Popovic T.; Rosenstein N.E.; Lake D.B.; Carlone G.M.; Mayer L.W.; Perkins B.A.; Rothrock G.; Mukergee N.; Daily P.; Gelling L.; Vugia D.; Barnes B.; Gilmore C.; Farley M.; Baughman W.; Whitfield S.; Bardsley M.; Billmann L.; Dwyer D.; Hadler J.; Mshar P.; Barrett N.; Morin C.; Phan Q.; Osterholm M.; Danila R.; Rainbow J.; Lexau C.; Triden L.; White K.; Besser J.; Stefonek K.; Donegon J.; Ladd-Wilson S.; Ajello G.; Berkowitz M.; Plikaytis B.; Reeves M.; Robinson K.; Schmink S.
CORPORATE SOURCE: M.L.C. Tondella, Respiratory Diseases Branch, Div. of Bacterial and Mycotic Dis., NCID, 1600 Clifton Rd., Atlanta, GA 30333, United States. MLT5@CDC.GOV
SOURCE: Journal of Clinical Microbiology, (2000) 38/9 (3323-3328). Refs: 39
ISSN: 0095-1137 CODEN: JCMIDW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Because the **Neisseria** meningitidis serogroup B (NMSB) capsule is poorly immunogenic in humans, immunization strategies have focused on noncapsular antigens. Both PorA and to a lesser extent PorB are noncapsular protein antigens capable of inducing protective bactericidal antibodies, and vaccines based on the outer membrane protein (OMP) components of serogroup B meningococci have been shown to be effective in clinical trials. Multiple PorA antigens seem to be needed to prevent endemic meningococcal disease around the world, and a hexavalent PorA-based meningococcal vaccine has recently been developed in The Netherlands. To evaluate the distribution of NMSB PorA and PorB antigens in the United States, serosubtyping and serotyping were done on 444 NMSB strains isolated in the active surveillance areas of the United States (total population, 32 million) during the period 1992 to 1998. A total of 244 strains were isolated from sporadic cases of meningococcal disease, and 200 strains were isolated from an epidemic in Oregon. A panel of 16 mouse monoclonal antibodies reactive with PorA and 15 monoclonal antibodies reactive with PorB were used. Among the NMSB isolates obtained from sporadic cases, the most prevalent serosubtypes were P1.7,16 (14.3%), P1.19,15 (9.8%), P1.7,1 (8.6%), P1.5,2 (7.8%), P1.22a, 14 (7.8%), and P1.14 (5.3%) and the most prevalent serotypes were 4,7 (27.5%), 15 (16%), 14 (8.6%), 10 (6.1%), 1 (4.9%), and 2a (3.7%). A multivalent PorA-based OMP vaccine aimed at the six most prevalent serosubtypes could have targeted about half of the sporadic cases of NMSB disease that occurred between 1992 and 1998 in the surveillance areas. Twenty serosubtypes would have had to be included in a multivalent vaccine to achieve 80% coverage of strains causing sporadic disease. The relatively large number of isolates that did not react with routine monoclonal antibodies indicates that DNA sequence-based variable region typing of NMSB will be necessary to provide precise information on the distribution and diversity of PorA antigens and correlation with nonserosubtypeable isolates. The high degree of variability observed in the PorA and PorB proteins of NMSB in the United States suggests that vaccine strategies not based on OMPs should be

further investigated.

L125 ANSWER 33 OF 57 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999185630 EMBASE
TITLE: Antigenic and molecular conservation of the gonococcal **NspA** protein.
AUTHOR: Plante M.; Cadieux N.; Rioux C.R.; Hamel J.; Brodeur B.R.; Martin D.
CORPORATE SOURCE: D. Martin, Unite de Recherche en Vaccinologie, Ctr. Hosp. Universitaire de Quebec, Pavillon CHUL, 2705 Blvd. Laurier, Ste-Foy, Que. G1V 4G2, Canada.
Denis.Martin@crchul.ulaval.ca
SOURCE: Infection and Immunity, (1999) 67/6 (2855-2861).
Refs: 44
ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A low-molecular-weight protein named **NspA** (neisserial surface protein A) was recently identified in the outer membrane of all **Neisseria** meningitidis strains tested. Antibodies directed against this protein were shown to protect mice against an experimental meningococcal infection. Hybridization experiments clearly demonstrated that the **nspA** gene was also present in the genomes of the 15 **Neisseria** gonorrhoeae strains tested. Cloning and sequencing of the **nspA** gene of N. gonorrhoeae B2 revealed an open reading frame of 525 nucleotides coding for a polypeptide of 174 amino acid residues, with a calculated molecular weight of 18,316 and a pI of 10.21. Comparison of the predicted amino acid sequence of the **NspA** polypeptides from the gonococcal strains B2 and FA1090, together with that of the meningococcal strain 608B, revealed an identity of 93%, suggesting that the **NspA** protein is highly conserved among pathogenic **Neisseria** strains. The level of identity rose to 98% when only the two gonococcal predicted **NspA** polypeptides were compared. To evaluate the level of antigenic conservation of the gonococcal **NspA** protein, monoclonal antibodies (MAbs) were generated. Four of the seven **NspA**-specific MAbs described in this report recognized their corresponding epitope in 100% of the 51 N. gonorrhoeae strains tested. Radioimmunobinding assays clearly indicated that the gonococcal **NspA** protein is exposed at the surface of intact cells.

L125 ANSWER 34 OF 57 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97136602 EMBASE
DOCUMENT NUMBER: 1997136602
TITLE: Modulation of the biological activities of meningococcal endotoxins by association with outer membrane proteins is not inevitably linked to toxicity.
AUTHOR: Quakyi E.K.; Hochstein H.D.; Tsai C.M.
CORPORATE SOURCE: E.K. Quakyi, Biologics Evaluation/Research Center, Food and Drug Administration, Bethesda, MD 20892, United States
SOURCE: Infection and Immunity, (1997) 65/5 (1972-1979).
Refs: 45
ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
AB Meningococcal sepsis results partly from overproduction of host cytokines after macrophages interact with endotoxin. To obtain less toxic and highly immunomodulatory meningococcal endotoxins for prophylactic purposes, we investigated the relationship between endotoxicity and immunomodulatory activity of several endotoxin preparations from **Neisseria** meningitidis group B. Using the D-galactosamine-sensitized mouse model to determine endotoxin lethality, we found that the toxicity of purified lipooligosaccharide (LOS) from M986, a group B disease strain, was three to four times higher than those of purified LOSs from the noncapsulated strains M986-NCV-1 and OP-, the truncated-LOS mutant. The LOSs of outer membrane vesicles (OMVs) and detergent-treated OMVs (D-OMVs) from the three strains were 2 to 3 and over 300 times less toxic than the purified LOSs, respectively. Intraperitoneal administration of these preparations induced production of tumor necrosis factor alpha (TNF-.alpha.) and interleukin 6 (IL-6) in serum 2 h after injections. However, repeated doses of low- and high- toxicity preparations induced lower amounts of TNF-.alpha. and IL-6, i.e., LOS tolerance. Injection of mice with low doses of LOS was as effective as injection with high doses in inducing tolerance. Peritoneal macrophages from tolerant mice pretreated with either high- or low-toxicity LOS preparations produced only a fraction of the amounts of TNF-.alpha. and IL-6 produced by control groups in response to LOS ex vivo. Despite tolerance to LOS induced by pretreatment with reduced-toxicity preparations, killing of N. meningitidis M986 by macrophages from these animals was enhanced. Protection was achieved when mice treated with LOS, and especially that of D-OMVs, were challenged with live N. meningitidis. The least toxic LOS, that in D-OMVs, was most effective in inducing hyporesponsiveness to endotoxin in mice but protected them against challenge with N. meningitidis. No inevitable link between toxicity and host immune modulation and responses was shown. Our results show that LOS is responsible for both toxicity and immunomodulation. When LOS is tightly associated with outer membrane proteins in D-OMV, it reduces toxicity but enhances beneficial effects compared to results with its purified form. Thus, systematic and critical evaluation of D-OMVs as adjuvants or as portions of group B meningococcal vaccines may help improve survival and outcome in meningococcal sepsis.

L125 ANSWER 35 OF 57 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94326749 EMBASE
DOCUMENT NUMBER: 1994326749
TITLE: Current status of meningococcal group B vaccine candidates: Capsular or noncapsular?.
AUTHOR: Diaz Romero J.; Outschoorn J.M.
CORPORATE SOURCE: Unidad de Respuesta Immune, Ctr Nacional Biologia Cel Retrovirus, Instituto de Salud Carlos III,Majadahonda, Madrid 28220, Spain
SOURCE: Clinical Microbiology Reviews, (1994) 7/4 (559-575). ISSN: 0893-8512 CODEN: CMIREX
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
008 Neurology and Neurosurgery
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Meningococcal meningitis is a severe, life-threatening infection for which no adequate vaccine exists. Current vaccines, based on the group-specific capsular polysaccharides, provide short-term protection in adults against serogroups A and C but are ineffective in infants and do not induce

protection against groups B strains, the predominant cause of infection in western countries, because the purified serogroup B polysaccharide fails to elicit human bactericidal antibodies. Because of the poor imunogenicity of group B capsular polysaccharide, different noncapsular antigens have been considered for inclusion in a vaccine against this serogroup: outer membrane proteins, lipooligosaccharides, iron-regulated proteins, Lip, pili, CtrA, and the immunoglobulin A proteases. Alternatively, attempts to increase the immunogenicity of the capsular polysaccharide have been made by using noncovalent complexes with outer membrane proteins, chemical modifications, and structural analogs. Here, we review the strategies employed for the development of a vaccine for **Neisseria** meningitidis serogroup B; the difficulties associated with the different approaches are discussed.

L125 ANSWER 36 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:452494 BIOSIS
DOCUMENT NUMBER: PREV200200452494
TITLE: **Immunization** with the recombinant PorB outer membrane protein induces a bactericidal immune response against **Neisseria** meningitidis.
AUTHOR(S): Wright, J. Claire; Williams, Jeannette N.; Christodoulides, Myron; Heckels, John E. (1)
CORPORATE SOURCE: (1) Molecular Microbiology and Infection, Division of Infection, Inflammation and Repair, Southampton General Hospital, University of Southampton Medical School, Tremona Road, Mailpoint 814, SO16 6YD, Southampton: jeh@soton.ac.uk UK
SOURCE: Infection and Immunity, (August, 2002) Vol. 70, No. 8, pp. 4028-4034. print.
ISSN: 0019-9567.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Infections with **Neisseria** meningitidis are characterized by life-threatening **meningitis** and septicemia. The meningococcal **porin** proteins from serogroup B meningococci have been identified as candidates for inclusion in **vaccines** to prevent such infections. In this study, we investigated the **vaccine** potential of the PorB **porin** protein free of other meningococcal components. The porB gene from a strain of **Neisseria** meningitidis expressing the class 3 outer membrane **porin** protein (PorB3) was cloned into the pRSETB vector, and the protein was expressed at high levels in a heterologous host Escherichia coli. The recombinant protein was purified to homogeneity by affinity chromatography and used for **immunization** after incorporation into liposomes and into micelles composed either of zwitterionic detergent or nondetergent sulfobetaine. The immunogenicity of these preparations was compared to recombinant PorB protein adsorbed to Al(OH)3 adjuvant as a control. Although sera raised against the protein adsorbed to Al(OH)3 reacted with the purified recombinant protein, sera raised against liposomes and micelles showed greater activity with native protein, as measured by enzyme immunoassay with outer membranes and by whole-cell immunofluorescence. Reactivity with native protein was considerably enhanced by incorporation of the adjuvant monophosphoryl lipid A into the liposome or micelle preparations. Recognition of the native protein was in a serotype-specific manner and was associated with the ability of the antisera to promote high levels of serotype-specific complement-mediated killing of meningococci. These results demonstrate that the PorB protein should be considered as a component of a **vaccine** designed to prevent serogroup B meningococcal infection.

L125 ANSWER 37 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:233208 BIOSIS
DOCUMENT NUMBER: PREV200100233208
TITLE: **Rational** design of a subtype-specific peptide **vaccine** against **Neisseria meningitis**.
AUTHOR(S): Oomen, Clasien J. (1); Bonvin, Alexandre M. J. J.; Haseley, Simon R.; Hoogerhout, Peter; van Alphen, Loek; Kroon, Jan (1); Gros, Piet (1)
CORPORATE SOURCE: (1) Department of Crystal and Structural Chemistry, Bijvoet Center for Biomolecular Research, Utrecht University, 3584 CH, Utrecht Netherlands
SOURCE: Fields, Gregg B.; Tam, James P.; Barany, George. (2000) pp. 702-703. Peptides for the new millennium. print.
Publisher: Kluwer Academic Publishers 3300 AA, Dordrecht, Netherlands.
Meeting Info.: 16th American Peptide Symposium Minneapolis, MI, USA June 26-July 01, 1999
ISBN: 0-7923-6445-7 (cloth).
DOCUMENT TYPE: Book; Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L125 ANSWER 38 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:325265 BIOSIS
DOCUMENT NUMBER: PREV200000325265
TITLE: Induction of antimeningitis immunity by the synthetic peptides. I. The immunoactive synthetic fragments of **porin** A from **Neisseria** meningitidis.
AUTHOR(S): Koroev, D. O. (1); Kotelnikova, O. V.; Volpina, O. M.; Zhmak, M. N.; Kupriyanova, M. A.; Agafonova, S. A.; Alliluev, A. P.; Litvinov, I. S.; Nesmeyanov, V. A.; Ivanov, V. T.
CORPORATE SOURCE: (1) Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, ul. Miklukho-Maklaya 16/10, GSP-7, Moscow, 117871 Russia
SOURCE: Bioorganicheskaya Khimiya, (May, 2000) Vol. 26, No. 5, pp. 323-329. print.
ISSN: 0132-3423.
DOCUMENT TYPE: Article
LANGUAGE: Russian
SUMMARY LANGUAGE: English; Russian
AB Fourteen peptides corresponding to sequences of all the exposed and some of the transmembrane protein regions of **porin** A from the outer membrane of **Neisseria** meningitidis strain B:15:P1.7,16 were synthesized. Mice of various lines were **immunized** with the free peptides not conjugated with any protein carrier. It was shown that the majority of the peptides possess immunogenic properties. Two peptides were identified binding to antibodies present in the serum of mice after **meningitis**. Protective properties of a number of the synthesized peptides were studied, and three peptide sequences inducing mice protection from an experimental infection with N. meningitidis were identified.

L125 ANSWER 39 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:155392 BIOSIS
DOCUMENT NUMBER: PREV200000155392
TITLE: Expression **library immunization** to identify protective antigens from **Neisseria** meningitidis.
AUTHOR(S): Boffey, J. (1); Mitchell, T. J. (1)
CORPORATE SOURCE: (1) Division of Infection and Immunity, Institute of

Biomedical and Life Sciences, University of Glasgow, Glasgow, G12 8QQ UK
SOURCE: Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 128. Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology . ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L125 ANSWER 40 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:107156 BIOSIS
DOCUMENT NUMBER: PREV199799406359
TITLE: Preclinical evaluation of a novel group B meningococcal conjugate **vaccine** that elicits bactericidal activity in both mice and nonhuman primates.
AUTHOR(S): Fusco, Peter C.; Michon, Francis (1); Tai, Joseph Y.; Blake, M. S.
CORPORATE SOURCE: (1) North American Vaccine Inc., 12103 Indian Creek Ct., Beltsville, MD 20705 USA
SOURCE: Journal of Infectious Diseases, (1997) Vol. 175, No. 2, pp. 364-372.
ISSN: 0022-1899.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Group B meningococcal (GBM) conjugate **vaccines** were prepared using chemically modified N-propionylated polysialic acid, from Escherichia coli K1 polysaccharide capsule, coupled by reductive amination to tetanus toxoid and purified recombinant GBM **porin** (rPorB). All conjugates elicited high antibody levels in mice with good booster responses. However, only rPorB conjugates elicited bactericidal activity specific against a broad spectrum of five different GBM serotypes. Bactericidal activity was completely inhibited by free N-propionylated polysaccharide. In baboons and rhesus monkeys, rPorB conjugates elicited high antibody titers, with IgG booster responses 9- to 15-fold higher than primary responses. Bactericidal activity increased 19- to 39-fold over preimmune values, using rabbit complement; increased bactericidal activity was also confirmed with human and monkey complement. IgG cross-reactivity for unmodified N-acetyl polysaccharide was lt 5% for 79% of mice and lt 10% for 80% of primates. These studies strongly suggest that the N-propionylated polysialic acid-rPorB conjugate is an excellent **vaccine** candidate for human use.

L125 ANSWER 41 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:454532 BIOSIS
DOCUMENT NUMBER: PREV199799753735
TITLE: Bactericidal antibody recognition of a PorA epitope of **Neisseria** meningitidis: Crystal structure of a Fab fragment in complex with a fluorescein-conjugated peptide.
AUTHOR(S): Van Den Elsen, Jean M. H.; Herron, James N.; Hoogerhout, Peter; Poolman, Jan T.; Boel, Edwin; Logtenberg, Ton; Wilting, Jaap; Crommelin, Daan J. A.; Kroon, Jan; Gros, Piet (1)
CORPORATE SOURCE: (1) Dep. Crystal Structural Chemistry, Utrecht University, Padualaan 8, 3584 CH-Utrecht Netherlands
SOURCE: Proteins Structure Function and Genetics, (1997) Vol. 29, No. 1, pp. 113-125.
ISSN: 0887-3585.
DOCUMENT TYPE: Article

LANGUAGE: English
AB Class 1 outer membrane protein PorA of **Neisseria** meningitidis is a **vaccine** candidate against bacterial **meningitis**. Antibodies against PorA are able to induce complement-mediated bacterial killing and thereby play an important role in protection against meningococcal disease. Bactericidal antibodies are all directed against variable regions VR1 and VR2 of the PorA sequence, corresponding to loops 1 and 4 of a two-dimensional topology model of the **porin** with eight extracellular loops. We have determined the crystal structure to 2.6 ANG resolution of the Fab fragment of bactericidal antibody MN12H2 against meningococcal PorA in complex with a linear fluorescein-conjugated peptide TKDTNNNL derived from the VR2 sequence of sero-subtype P1.7,16 (residues 180-187) from meningococcal strain H44/76. The peptide folds deeply into the binding cavity of the Fab molecule in a type I beta-turn, with the minimal P1.16 epitope DTNNN virtually completely buried. The structure reveals H-bonds and van der Waals interactions with all minimal epitope residues and one essential salt bridge between Asp-182 of the peptide and His-31 of the MN12H2 light chain. The key components of the recognition of PorA epitope P1.16 by bactericidal antibody MN12H2 correspond well with available thermodynamic data from binding studies. Furthermore, they indicate the structural basis of an increased endemic incidence of infection by group B meningococci in England and Wales since 1981 associated with the occurrence of an **Neisseria** meningitidis escape mutant (strain MC58). The observed three-dimensional conformation of the peptide provides a rationale for the development of a synthetic peptide **vaccine** against meningococcal disease.

L125 ANSWER 42 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:509210 BIOSIS
DOCUMENT NUMBER: PREV199699231566
TITLE: Immune responses to linear epitopes on the PorB protein of **Neisseria** meningitidis in patients with systemic meningococcal disease.
AUTHOR(S): Delvig, Alexei A. (1); Wedege, Elisabeth; Michaelsen, Terje E.; Hoiby, E. Arne; Brandntzaeg, Petter; Rosenqvist, Einar
CORPORATE SOURCE: (1) National Inst. Public Health, Dep. Vaccinol., N-0403 Oslo Norway
SOURCE: Microbiology (Reading), (1996) Vol. 142, No. 9, pp. 2491-2498.
ISSN: 1350-0872.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Neisserial **porins**, the major protein constituents of the outer membrane capable of inducing antibody responses in humans, are considered to be meningococcal **vaccine** candidates, so it is important to map the relevant B-cell epitopes. For B-cell epitope analyses of the serotype 15 PorB protein in **Neisseria meningitis**, paired sera from selected patients with systemic meningococcal disease (SMD) were screened with synthetic 12mer peptides spanning the PorB protein sequence, and/or its variable region 1 (VR1). A 'SMD-related' linear B-cell epitope was found within the VR1 region consisting of 14 residues (17svFHQNGQVTEvtt-30). A 23mer soluble peptide (D63b2) that covered the VR1 region, including the complete 17svFHQNGQVTEvtt-30 sequence, was recognized, whereas no detectable binding was observed to a 16mer peptide (D63a1) containing most of the essential sequence (19FHQNGQVTEvtt-30). A low frequency of IgG responses specific for the PorB linear epitopes was found in convalescent-phase sera from 132 SMD patients studied, as judged from both immunoblotting studies (24/132; 18-2%) and reactivity with peptide D63b2 (18/132; 13-6%). Peptide D63b2 significantly inhibited IgG binding to the denatured PorB protein on immunoblots, suggesting that this B-cell epitope was one of the main

linear epitopes on the PorB protein recognized by sera from some SMD patients.

L125 ANSWER 43 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:523272 BIOSIS
DOCUMENT NUMBER: PREV199396136679
TITLE: Use of transformation to construct antigenic hybrids of the class 1 outer membrane protein in **Neisseria** meningitidis.
AUTHOR(S): Van Der Ley, Peter (1); Van Der Biezen, Jenny; Hohenstein, Peter; Peeters, Carla; Poolman, Jan T.
CORPORATE SOURCE: (1) Natl. Inst. Public Health and Environ. Protection, Antonie van Leeuwenhoeklaan 9, P.O. Box 3720 BA Bilthoven Netherlands Antilles
SOURCE: Infection and Immunity, (1993) Vol. 61, No. 10, pp. 4217-4224.
ISSN: 0019-9567.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The class 1 protein of **Neisseria** meningitidis is an important component of candidate outer membrane **vaccines** against meningococcal **meningitis**. This **porin** protein contains two variable regions which determine subtype specificity and provide binding sites for bactericidal monoclonal antibodies. To determine the contribution of each of these variable regions in the induction of bactericidal antibodies, a set of isogenic strains differing only in their class 1 epitopes was constructed. This was done by transformation of meningococcal strain H44/76 with cloned class 1 genes and selection of the desired epitope combinations in a colony blot with subtype-specific monoclonal antibodies. When used for the **immunization** of mice, outer membrane complexes induced bactericidal antibodies only against meningococcal strains sharing at least one of their class 1 epitopes. The results demonstrate that the P1.2 and P1.16 epitopes, normally located in the fourth exposed loop of the protein, efficiently induce bactericidal antibodies independently of the particular sequence in the first variable region. The P1.5 and P1.7 epitopes, normally located in the first exposed loop, were found to induce lower bactericidal titers. Hybrid class 1 outer membrane proteins were constructed by inserting oligonucleotides encoding the P1.7 and P1.16 epitopes into the porA gene. In this way, we obtained a set of strains which carry the P1.5 epitope in loop 1, P1.2 in loop 4, and P1.7 and P1.16 (separately or in combination) in either loop 5 or loop 6. The additional epitopes were found to be exposed at the cell surface. Outer membrane complexes from several of these strains were found to induce a bactericidal response in mice against the inserted epitopes. These results demonstrate that it is feasible to construct meningococcal strains carrying multivalent class 1 proteins in which multiple subtype-specific epitopes are present in different cell surface-exposed loops.

L125 ANSWER 44 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:134664 BIOSIS
DOCUMENT NUMBER: PREV199497147664
TITLE: A rapid and sensitive PCR strategy employed for amplification and sequencing of porA from a single colony-forming unit of **Neisseria** meningitidis.
AUTHOR(S): Saunders, Nancy B.; Zollinger, Wendell D.; Rao, Venigalla B. (1)
CORPORATE SOURCE: (1) Dep. Biol., 103 McCort Ward Hall, Catholic Univ. America, 620 Michigan Ave. N.E., Washington, DC 20064 USA
SOURCE: Gene (Amsterdam), (1993) Vol. 137, No. 2, pp. 153-162.
ISSN: 0378-1119.

DOCUMENT TYPE: Article
LANGUAGE: English
AB The predicted amino acid sequence was determined for the class-1 outer membrane protein, PorA, from a B:15:P1.7,3 strain of **Neisseria** meningitides that is currently causing an epidemic of **meningitis** in Northern Chile. The P1.7,3 PorA showed a unique sequence in the exposed loop 4 of the putative **porin** structure that is different from all the reported PorA sequences. Based on the nucleotide (nt) sequence of the P1.7,3 porA, we designed two sets of PCR (polymerase chain reaction) primers that specifically amplified porA from any N. meningitides strain, and a third set of primers that amplified porA only from the P1.7,3 strain. Using these primers, we developed a sensitive double hot-start nested PCR (HNPCR) strategy that could amplify porA and generate nt sequence from as low as a single colony-forming unit. This strategy consisted of three phases of PCR. The first two phases were designed to generate amplified target DNA that could be directly visualized by ethidium bromide staining starting from one to two molecules of **Neisseria** genome. The third phase was designed to generate a sequence of several hundred nt directly from the amplified DNA. A number of culture-negative cerebrospinal fluid samples from individuals suspected of **meningitis** during a **vaccine** trial were analyzed by this strategy to obtain more accurate information on the actual number of cases that occurred in the study and the non-study populations. The basic HNPCR strategy described here could be applied to amplify and sequence target DNAs from any low-copy-number biological sample.

L125 ANSWER 45 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1991:501865 BIOSIS
DOCUMENT NUMBER: BA92:124825
TITLE: T CELL RECOGNITION OF **NEISSERIA**-MENINGITIDIS CLASS 1 OUTER MEMBRANE PROTEINS IDENTIFICATION OF T CELL EPITOPES WITH SELECTED SYNTHETIC PEPTIDES AND DETERMINATION OF HLA RESTRICTION ELEMENTS.
AUTHOR(S): WIERTZ E J H J; VAN GAANS-VAN DEN BRINK J A M; SCHREUDER G M T H; TERMIJTELEN A A M; HOOGERHOUT P; POOLMAN J T
CORPORATE SOURCE: NATL. INST. PUBLIC HEALTH ENVIRONMENTAL PROTECTION, P.O. BOX 1, 3720 BA BILTHOVEN, NETH.
SOURCE: J IMMUNOL, (1991) 147 (6), 2012-2018.
CODEN: JOIMA3. ISSN: 0022-1767.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB No **vaccine** is yet available against serogroup B meningococci, which are a common cause of bacterial **meningitis**. Some outer membrane proteins (OMP), LPS, and capsular polysaccharides have been identified as protective Ag. The amino acid sequence of the protective B cell epitopes present within the class 1 OMP has been described recently. Synthetic peptides containing OMP B cell epitopes as well as capsular polysaccharides or LPS protective B cell epitopes have to be presented to the immune system in association with T cell epitopes to achieve an optimal Ir. The use of homologous, i.e., meningococcal, T cell epitopes has many advantages. We therefore investigated recognition sites for human T cells within the meningococcal class 1 OMP. We have synthesized 16 class 1 OMP-derived peptides encompassing predicted T cell epitopes. Peptides corresponding to both surface loops and trans-membrane regions (some of which occurs as amphipathic .beta.-sheets) of the class 1 OMP were found to be recognized by T cells. In addition, 10 of 11 peptides containing predicted amphipathic .alpha.-helices and four of five peptides containing T cell epitope motifs according to Rothbard and Taylor (Rothbard, J. B., and W. R. Taylor. 1988. EMBO J 7:93) were recognized by lymphocytes from one or more volunteers. Some of the T and B cell epitopes were shown to map to identical regions of the protein. At least six of the peptides that

were found to contain T cell epitopes show homology to constant regions of the meningococcal class 3 OMP and the gonococcal **porins** PIA and PIB. Peptide-specific T cells lines and T cell clones were established to investigate peptide recognition in more detail. The use of a panel of HLA-type APC revealed clear HLA-DR restriction patterns. It seems possible now to develop a (semi-) synthetic meningococcal **vaccine** with a limited number of constant T cell epitopes that cover all HLA-DR locus products.

L125 ANSWER 46 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-451895 [48] WPIDS
DOC. NO. CPI: C2001-136558
TITLE: Composition for treating or preventing infection to, detecting, or for raising antibodies against Neisserial bacteria, comprises an N. meningitidis serogroup B outer membrane preparation and an immunogenic component.
DERWENT CLASS: B04 D16
INVENTOR(S): GIULIANI, M; PIZZA, M; RAPPUOLI, R
PATENT ASSIGNEE(S): (CHIR-N) CHIRON SPA
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001052885	A1	20010726	(200148)*	EN	81
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001028754	A	20010731	(200171)		
EP 1248647	A1	20021016	(200276)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001052885	A1	WO 2001-IB166	20010117
AU 2001028754	A	AU 2001-28754	20010117
EP 1248647	A1	EP 2001-942562	20010117
		WO 2001-IB166	20010117

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001028754	A	Based on	WO 200152885
EP 1248647	A1	Based on	WO 200152885

PRIORITY APPLN. INFO: GB 2000-5699 20000309; GB 2000-1067 20000117

AB WO 200152885 A UPAB: 20010829
NOVELTY - A composition (C) comprising an **Neisseria** meningitidis serogroup B outer membrane preparation and an immunogenic component, is new.

DETAILED DESCRIPTION - A new composition (C) comprises a **Neisseria** meningitidis serogroup B outer membrane preparation and an immunogenic component that is a protein disclosed in WO99/57280,

WO99/36544, WO99/24578, WO99/66791, WO97/28273, WO96/29412, WO95/03413, WO99/31132, WO99/58683, WO99/55873, Tettelin et al, Science 287:1890-1815 (2000), and/or N. meningitidis protein PorA, **TbpA**, **TbpB** , PilC, OpA, or Omp85.

INDEPENDENT CLAIMS are also included for the following:

(1) use of (C) in the manufacture of:

(i) a medicament for treating or preventing infection due to Neisserial bacteria;

(ii) a diagnostic reagent for detecting the presence of Neisserial bacteria or of antibodies raised against Neisserial bacteria; and/or

(iii) a reagent which can raise antibodies against Neisserial bacteria;

(2) treating a patient comprising administering (C); and

(3) a bacterial outer membrane preparation comprising an immunogenic component selected from one of those in (C).

ACTIVITY - Virucide; antibacterial; antitussive; antiinflammatory. No suitable biological data is given.

MECHANISM OF ACTION - **Vaccine** (claimed).

USE - (C) is used for manufacturing:

(a) a medicament for treating or preventing infection due to Neisserial bacteria;

(b) a diagnostic reagent for detecting the presence of Neisserial bacteria or of antibodies raised against Neisserial bacteria; and/or

(c) a reagent which can raise antibodies against Neisserial bacteria (claimed).

(C) is used a **vaccine** (claimed).

Dwg.0/0

L125 ANSWER 47 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-138654 [14] WPIDS
CROSS REFERENCE: 2002-188688 [24]
DOC. NO. CPI: C2001-041027
TITLE: New isolated polynucleotide useful for outer membrane vesicle preparation from Gram-negative bacterial strain for **vaccination** of microbial infections.
DERWENT CLASS: B04 D16
INVENTOR(S): BERTHET, F J; DALEMANS, W L J; DENOEL, P; DEQUESNE, G; FERON, C; LOBET, Y; POOLMAN, J; THIRY, G; THONNARD, J; VOET, P; DALEMANS, W L; LHONNARD, J
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (SMIK) SMITHKLINE BEECHAM BIOLOGICALS SA
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001009350	A2	20010208	(200114)*	EN	127
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000068336	A	20010219	(200129)		
NO 2002000506	A	20020402	(200235)		
BR 2000012974	A	20020507	(200238)		
CZ 2002000403	A3	20020515	(200241)		
EP 1208214	A2	20020529	(200243)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
KR 2002027514	A	20020413	(200267)		

HU 2002003056 A2 20021228 (200308)
CN 1377415 A 20021030 (200314)
JP 2003506049 W 20030218 (200315) 189

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001009350	A2	WO 2000-EP7424	20000731
AU 2000068336	A	AU 2000-68336	20000731
NO 2002000506	A	WO 2000-EP7424	20000731
		NO 2002-506	20020131
BR 2000012974	A	BR 2000-12974	20000731
		WO 2000-EP7424	20000731
CZ 2002000403	A3	WO 2000-EP7424	20000731
		CZ 2002-403	20000731
EP 1208214	A2	EP 2000-956369	20000731
		WO 2000-EP7424	20000731
KR 2002027514	A	KR 2002-701441	20020201
HU 2002003056	A2	WO 2000-EP7424	20000731
		HU 2002-3056	20000731
CN 1377415	A	CN 2000-813842	20000731
JP 2003506049	W	WO 2000-EP7424	20000731
		JP 2001-514142	20000731

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000068336	A	Based on	WO 200109350
BR 2000012974	A	Based on	WO 200109350
CZ 2002000403	A3	Based on	WO 200109350
EP 1208214	A2	Based on	WO 200109350
HU 2002003056	A2	Based on	WO 200109350
JP 2003506049	W	Based on	WO 200109350

PRIORITY APPLN. INFO: GB 1999-18319 19990803

AB WO 200109350 A UPAB: 20030303
NOVELTY - An isolated polynucleotide sequence which hybridizes under highly stringent conditions to at least a 30 nucleotide portion of 80 sequences described in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) a genetically-engineered outer membrane vesicle (bleb) preparation from a Gram-negative bacterial strain characterized in that the preparation is obtainable by employing a process comprising:

(a) introducing a heterologous gene, optionally controlled by a strong promoter sequence, into the chromosome by homologous recombination; and

(b) making blebs from the strain;

(2) a **vaccine** comprising a bleb preparation and a pharmaceutically acceptable excipient;

(3) a vector suitable for performing recombination events;

(4) a modified Gram-negative bacterial strain from which the bleb preparation is made;

(5) an immuno-protective and non-toxic Gram-negative bleb, ghost, or killed whole cell **vaccine** suitable for paediatric use.

ACTIVITY - Antiviral; Antibacterial; Antifungal.

Animals were **immunized** three times with 5 micro g of the different OMVs absorbed on Al(OH)3 on days 0, 14, and 28. Bleedings were done on days 28 and 35, and they were challenged on day 35. The challenge dose was 20 X LD50 (approx. 10 to the power of 7 CFU/mouse). Mortality

rate was monitored for 7 days after challenge.
OMVs injected were:
Group1: Cps-, PorA+
Group2: Cps-, PorA-
Group3: Cps-, PorA-, **NspA**+
Group4: Cps-, PorA-, Omp85+
Group5: Cps-, PorA-, Hsf+
24 hours after the challenge, there was 100% mortality in the negative control group, while mice **immunized** with the 5 different OMVs preparations were still alive. Sickness was also monitored during the 7 days and the mice **immunized** with the **NSPA** over-expressed blebs appeared to be less sick than the other groups. PorA present in PorA+ blebs is likely to confer extensive protection against infection by the homologous strain. However, protection induced by PorA-up-regulated blebs is likely to be due at least to some extent, to the presence of increased amount of **NspA**, OMP85 or Hsf.
MECHANISM OF ACTION - **Vaccine**.
USE - The claimed polynucleotide sequence is used in performing a homologous recombination event within 1000 base pairs upstream of a Gram-negative bacterial chromosomal gene in order to either increase or decrease expression of the gene. The bleb preparation is useful in the manufacture of a medicament for **immunizing** a human host against a disease caused by infection of one or more of the following: **Neisseria** meningitidis, **Neisseria** gonorrhoeae, Haemophilus influenza, Moraxella catarrhalis, Pseudomonas aeruginosa, Chlamydia trachomatis, and Chlamydia pneumonia. The invention is useful for **immunizing** a human host against the diseases caused by the above. The invention also provides **immunization** against the influenza virus. Immuno-protective and non-toxic Gram-negative bleb, ghost, or killed whole cell **vaccines** are useful for paediatric use (all claimed).
ADVANTAGE - The **vaccine** is more immunogenic, less toxic, and safer.
Dwg.0/17

L125 ANSWER 48 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-025167 [03] WPIDS
DOC. NO. CPI: C2001-007780
TITLE: Novel composition comprising first and second biological molecules from a **Neisseria** bacterium, useful as **vaccines** or immunogenic compositions for treating Neisserial infections.
DERWENT CLASS: B04 D16
INVENTOR(S): GIULIANI, M M; PIZZA, M; RAPPUOLI, R
PATENT ASSIGNEE(S): (CHIR-N) CHIRON SPA
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000071725	A2	20001130	(200103)*	EN	126
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000050977	A	20001212	(200115)		
EP 1179072	A2	20020213	(200219)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

BR 2000010721 A 20020611 (200248)
CN 1362992 A 20020807 (200304)
JP 2003500420 W 20030107 (200314) 151

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000071725	A2	WO 2000-IB828	20000519
AU 2000050977	A	AU 2000-50977	20000519
EP 1179072	A2	EP 2000-935438	20000519
		WO 2000-IB828	20000519
BR 2000010721	A	BR 2000-10721	20000519
		WO 2000-IB828	20000519
CN 1362992	A	CN 2000-810600	20000519
JP 2003500420	W	JP 2000-620102	20000519
		WO 2000-IB828	20000519

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000050977	A	Based on	WO 200071725
EP 1179072	A2	Based on	WO 200071725
BR 2000010721	A	Based on	WO 200071725
JP 2003500420	W	Based on	WO 200071725

PRIORITY APPLN. INFO: GB 2000-5730 20000309; GB 1999-11692 19990519; GB 1999-19705 19990819

AB WO 200071725 A UPAB: 20010124
NOVELTY - A composition (I) comprising first and second biological (B1 and B2) molecules from a **Neisseria** bacterium, is new.
ACTIVITY - Antibacterial. No supporting data is given.
MECHANISM OF ACTION - **Vaccine**.
USE - (I) is useful as a medicament (claimed), e.g. as immunogenic compositions or **vaccines** or as diagnostic reagents. (I) is used or treating or preventing infection due to Neisserial bacteria, as a diagnostic reagent for detecting the presence of Neisserial bacteria or of antibodies raised against Neisserial bacterial and/or a reagent which can raise antibodies against Neisserial bacteria. (I) is also useful for treating a patient infected with Neisserial bacteria infection.
Dwg.0/35

L125 ANSWER 49 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-647603 [62] WPIDS
CROSS REFERENCE: 2000-062150 [05]; 2000-318079 [27]; 2001-557776 [62]; 2001-582163 [65]
DOC. NO. CPI: C2000-195957
TITLE: **Neisseria** meningitidis B full length genome sequence and open **reading** frames are used to detect, treat and prevent Neisserial infections.
DERWENT CLASS: B04 D16
INVENTOR(S): FRAZER, C M; GALEOTTI, C; GRANDI, G; HICKEY, E; MASIGNANI, V; MORA, M; PETERSON, J; PIZZA, M; RAPPUOLI, R; RATTI, G; SCARLATO, V; SCARSELLI, M; TETTELIN, H; VENTER, J C
PATENT ASSIGNEE(S): (CHIR) CHIRON CORP; (GENO-N) INST GENOMIC RES
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

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WO 2000066791 A1 20001109 (200062)* EN  669
   RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
       OA PT SD SE SL SZ TZ UG ZW
    W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE
       ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
       LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK
       SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000032492 A  20001117 (200111)
EP 1185691    A1 20020313 (200225)  EN
    R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1359426    A  20020717 (200268)
```

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000066791	A1	WO 2000-US5928	20000308
AU 2000032492	A	AU 2000-32492	20000308
EP 1185691	A1	EP 2000-910392	20000308
		WO 2000-US5928	20000308
CN 1359426	A	CN 2000-809820	20000308

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000032492	A	Based on	WO 200066791
EP 1185691	A1	Based on	WO 200066791

PRIORITY APPLN. INFO: GB 2000-4695 20000228; US 1999-132068P 19990430; WO 1999-US23573 19991008

AB WO 200066791 A UPAB: 20021022

NOVELTY - A nucleic acid (I) comprising the full length genome of **Neisseria** meningitidis B (NMB) (II) or one or more NMB open reading frames, all given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for identifying an amino acid (aa) sequence comprising searching for putative open reading frames or protein coding sequences within (I);

(2) a method for producing a protein comprising expressing a protein comprising an aa sequence identified by the above method;

(3) a method for identifying a protein in N. meningitidis comprising producing a protein as in (2), producing an antibody which binds to the protein and determining whether the antibody recognizes a protein produced by N. meningitidis;

(4) nucleic acid comprising an open reading frame or protein coding sequence identified by the method of (1);

(5) a protein (V) obtained by the method of (2);

(6) a nucleic acid (II) comprising a fragment of (I);

(7) a nucleic acid (III) comprising a nucleotide sequence with greater than 50% sequence identity to (I);

(8) a nucleic acid complementary to (I), (II) or (III);

(9) a protein (VI) comprising an aa sequence encoded within (I);

(10) a protein (VII) comprising an aa sequence having greater then 50% sequence identity to an aa sequence encoded within (I);

(11) a protein (VIII) comprising a fragment of an aa sequence encoded within (I);

(12) nucleic acid (IV) encoding one of (VI)-(VIII);

(13) a computer, a computer memory, a computer storage medium or a

computer database containing (I), (II) or (III);

(14) a polyclonal or monoclonal antibody which binds to (VI)-(VIII) or (V);

(15) a nucleic acid probe comprising nucleic acid (I), (II), (III) or (IV); and

(16) an amplification primer comprising nucleic acid (I), (II), (III) or (IV).

ACTIVITY - Antibacterial.

No biological data is given.

MECHANISM OF ACTION - **Vaccine**; Gene therapy.

USE - Nucleic acids (I), (II), (III) or (IV), protein (VI)-(VIII) or (V) and/or antibody which binds to (VI)-(VIII) or (V) can be used in a composition for treating or preventing infection due to Neisserial bacteria or as a diagnostic reagent for detecting the presence of Neisserial bacteria or of antibodies raised to Neisserial bacteria (claimed).

The computer, computer memory, computer storage medium or computer database can be used in a search to identify open reading frames (ORFs) or coding sequences within (I).

ADVANTAGE - The DNA sequences provide further opportunities to find antigenic or immunogenic proteins which are more effective in **vaccines** than the **outer membrane proteins** currently used.

Dwg.0/18

L125 ANSWER 50 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-365400 [31] WPIDS
DOC. NO. CPI: C2000-110298
TITLE: Compositions for conferring protective immunity to Gram negative bacteria, especially **Neisseria** meningitidis, the causal agent of meningococcal meningitis, comprise both **transferrin binding** proteins A and B.
DERWENT CLASS: B04 D16
INVENTOR(S): GORRINGE, A R; HUDSON, M J; REDDIN, K M; ROBINSON, A
PATENT ASSIGNEE(S): (MICR-N) MICROBIOLOGICAL RES AUTHORITY
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000025811	A2	20000511	(200031)*	EN	26
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 2000010569	A	20000522	(200040)		
BR 9914946	A	20010710	(200142)		
EP 1126874	A2	20010829	(200150)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002528515	W	20020903	(200273)		31

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000025811	A2	WO 1999-GB3626	19991102
AU 2000010569	A	AU 2000-10569	19991102

BR 9914946	A	BR 1999-14946	19991102
		WO 1999-GB3626	19991102
EP 1126874	A2	EP 1999-954130	19991102
		WO 1999-GB3626	19991102
JP 2002528515	W	WO 1999-GB3626	19991102
		JP 2000-579250	19991102

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000010569	A	Based on	WO 200025811
BR 9914946	A	Based on	WO 200025811
EP 1126874	A2	Based on	WO 200025811
JP 2002528515	W	Based on	WO 200025811

PRIORITY APPLN. INFO: GB 1998-23978 19981102

AB WO 200025811 A UPAB: 20000630

NOVELTY - Compositions which confer improved protective immunity to Gram negative bacteria comprise both **transferrin binding** proteins (**Tbps**) A and B, or **Tbps** and other components.

DETAILED DESCRIPTION - The compositions may comprise:

(i) **transferrin binding** proteins A (**TbpA**) and B (**TbpB**);

(ii) a complex of two **TbpAs** and one **TbpB**;

(iii) **TbpA** and/or **TbpB** and N. meningitidis outer membrane vesicles; or (iv) **TbpA** and/or **TbpB** and a Cu,Zn-superoxide dismutase (Cu,Zn-SOD).

INDEPENDENT CLAIMS are also included for the following:

(1) a **vaccine** comprising a composition as above;

(2) a method of manufacturing the composition comprising combining a covalently linked complex of **TbpA** and **TbpA** with N. meningitidis outer membrane vesicles and a pharmaceutically acceptable carrier;

(3) a method of manufacturing a composition comprising combining a covalently linked complex of **TbpA** and **TbpB** with a Cu, Zn-SOD and a pharmaceutically acceptable carrier.

USE - The compositions (especially (i); claimed) are useful to treat Gram negative bacterial infections, especially with **Neisseria** meningitidis, the causal agent of meningococcal meningitis. They (especially (i); claimed) can be used to produce **vaccines** which can be administered to confer protective immunity to infection or protect against sub-clinical infection (i.e. where symptoms are not immediately apparent) with Gram negative bacteria; the **vaccines** are particularly useful to provide immunity to a broad spectrum of N. meningitidis strains simultaneously to protect against meningococcal disease.

ADVANTAGE - Compositions comprising **TbpA** plus **TbpB** provided higher protective immunity to meningococcal infection than prior art compositions comprising **TbpB** alone. The compositions of (iii) can also provide more effective and/or broader spectrum protection against N. meningitidis than existing **vaccines**, since they present a wider combination of N. meningitidis antigens, and the **Tbps** are presented in a highly antigenic environment that closely mimics that on live, infecting bacteria. Similarly, the compositions of (iv) additionally comprise Cu,Zn-SOD, which has previously been identified in the periplasm of Gram negative species, including N. meningitidis.

Dwg.0/7

L125 ANSWER 51 OF 57 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2001-060004 [07] WPIDS

DOC. NO. CPI: C2001-016523
TITLE: **Vaccine** for eliciting an immune response to N-acetylated gangliosides, useful for cancer treatment, comprises an immunogen noncovalently coupled to **Neisseria meningitis outer membrane protein** complex.
DERWENT CLASS: B04 D16
INVENTOR(S): HERNANDEZ, O G V; MOLINA, L E F; PEREZ, A C; RODRIGUEZ, G M; RODRIGUEZ, R P
PATENT ASSIGNEE(S): (IMMU-N) CENT IMMUNOLOGIA MOLECULAR
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6149921	A	20001121	(200107)*		8

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6149921	A	CIP of	US 1994-365684	19941229
			US 1998-61710	19980417

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6149921	A	CIP of	US 5788985

PRIORITY APPLN. INFO: CU 1997-130 19971110
AB US 6149921 A UPAB: 20010202
NOVELTY - **Vaccine** composition for stimulating or increasing an antibody immune response to N-acetylated gangliosides comprises:
(a) an immunogen coupled to **Neisseria meningitis outer membrane protein** complex (OMPC) by noncovalent hydrophobic interaction, selected from N-acetylated gangliosides and the corresponding oligosaccharides; and
(b) an adjuvant.
USE - The **vaccine** is useful for the prevention and treatment of cancer.
Dwg.0/0

L125 ANSWER 52 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-072624 [06] WPIDS
DOC. NO. NON-CPI: N2000-056803
DOC. NO. CPI: C2000-020804
TITLE: New isolated **Neisseria** meningitidis polypeptides and polynucleotides, used to develop products for the diagnosis, prevention and treatment of infections.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): RUELLE, J; TOMMASSEN, J P M
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (UYUT-N) RIJKSUNIV UTRECHT; (SMIK) SMITHKLINE BEECHAM BIOLOGICALS SA
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9961620	A2	19991202	(200006)*	EN	95

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG US UZ VN YU ZA ZW

AU 9945006 A 19991213 (200020)
BR 9911601 A 20010206 (200111)
NO 2000005952 A 20010118 (200112)
EP 1080198 A2 20010307 (200114) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
CZ 2000004395 A3 20010711 (200147)
KR 2001052409 A 20010625 (200173)
HU 2001002730 A2 20011128 (200209)
CN 1322249 A 20011114 (200217)
ZA 2000006872 A 20020327 (200230) 106
JP 2002516105 W 20020604 (200239) 101
NZ 508324 A 20020726 (200262)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9961620	A2	WO 1999-EP3603	19990526
AU 9945006	A	AU 1999-45006	19990526
BR 9911601	A	BR 1999-11601	19990526
		WO 1999-EP3603	19990526
NO 2000005952	A	WO 1999-EP3603	19990526
		NO 2000-5952	20001124
EP 1080198	A2	EP 1999-927754	19990526
		WO 1999-EP3603	19990526
CZ 2000004395	A3	WO 1999-EP3603	19990526
		CZ 2000-4395	19990526
KR 2001052409	A	KR 2000-713336	20001127
HU 2001002730	A2	WO 1999-EP3603	19990526
		HU 2001-2730	19990526
CN 1322249	A	CN 1999-809103	19990526
ZA 2000006872	A	ZA 2000-6872	19990526
JP 2002516105	W	WO 1999-EP3603	19990526
		JP 2000-551004	19990526
NZ 508324	A	NZ 1999-508324	19990526
		WO 1999-EP3603	19990526

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9945006	A	Based on	WO 9961620
BR 9911601	A	Based on	WO 9961620
EP 1080198	A2	Based on	WO 9961620
CZ 2000004395	A3	Based on	WO 9961620
HU 2001002730	A2	Based on	WO 9961620
JP 2002516105	W	Based on	WO 9961620
NZ 508324	A	Based on	WO 9961620

PRIORITY APPLN. INFO: GB 1998-11260 19980526

AB WO 9961620 A UPAB: 20010312
NOVELTY - A novel isolated polypeptide comprises an amino acid sequence which has at least 75% identity to an amino acid sequence selected from sequence (IV) and (VI) both having 769 residue amino acid sequences fully defined in the specification, comprising variants of the BASB030

polypeptide sequence.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an isolated polypeptide of sequence (II) having 769 amino acids, fully defined in the specification;

(2) an immunogenic fragment of a polypeptide as in the novelty or (1) in which the immunogenic activity of the immunogenic fragment is the same as a polypeptide of sequence (IV) or (VI);

(3) an isolated PN comprising a nucleotide sequence (NS) encoding a polypeptide that has at least 85% identity to an amino acid sequence (IV) or (VI) over its entire length, or an NS complementary to the isolated PN;

(4) an isolated PN comprising an NS that has at least 85% identity to an NS encoding a polypeptide of sequence (IV) or (VI) over its entire coding region, or an NS complementary to the isolated PN;

(5) an isolated PN which comprises an NS which has at least 85% identity to that of sequence (III) or (V) having 2310 nucleotides fully defined in the specification, over their entire lengths, or an NS complementary to the isolated PN;

(6) an isolated PN comprising a NS encoding a polypeptide of sequence (IV) or (VI), obtainable by screening an appropriate library under stringent hybridization conditions with a labeled probe having a sequence (III) or (V) or a fragment;

(7) an isolated PN comprising an NS encoding a polypeptide of sequence (II);

(8) an isolated PN comprising a PN of sequence (I) having 2310 nucleotides, fully defined in the specification;

(9) an isolated PN comprising an NS encoding a polypeptide of sequence (II), obtainable by screening an appropriate library under stringent hybridization conditions with a labeled probe having a sequence (I) or a fragment;

(10) an expression vector or a recombinant live microorganism comprising an isolated PN as in (3)-(9);

(11) a host cell comprising an expression vector as in (10) or a subcellular fraction or a membrane of the host cell expressing an isolated polynucleotide comprising an amino acid sequence that has at least 85% identity to an amino acid sequence selected from sequences (IV) or (VI);

(12) an antibody immunospecific for a polypeptide or immunological fragment as in the novelty or (1) or (2); and

(13) a method of diagnosing a **Neisseria** meningitidis infection, comprising identifying a polypeptide (I)-(VI), or an antibody immunospecific for them, present within a biological sample from an animal suspected of having the infection.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - **Vaccine**.

USE - The polypeptides or PNs can be used in **vaccine** compositions for preventing NM infections, e.g. bacteremia and **meningitis**. The antibodies can be used for treating NM disease. The products can also be used for diagnosis of disease, staging of disease or response of an infectious organism to drugs. The products can also be used for drug screening.

Dwg.0/8

L125 ANSWER 53 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1999-190036 [16] WPIDS
DOC. NO. CPI: C1999-055857
TITLE: **Vaccine** containing small subunit of human transferrin receptor from **Neisseria** meningitidis - for treatment and prevention of meningitis.
DERWENT CLASS: B04 D16
INVENTOR(S): QUENTIN-MILLET, M; ROKBI, B; QUENTIN, M M J
PATENT ASSIGNEE(S): (INMR) PASTEUR MERIEUX SERUMS & VACCINS SA

COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9907741	A1	19990218	(199916)*	FR	73
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
FR 2767060	A1	19990212	(199916)		
NO 9901558	A	19990330	(199927)		
AU 9889875	A	19990301	(199928)		
EP 948534	A1	19991013	(199947)	FR	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CN 1241193	A	20000112	(200022)		
MX 9903186	A1	19990801	(200063)		
JP 2001503068	W	20010306	(200116)		70
HU 2000001451	A2	20010428	(200131)		
NZ 334992	A	20010928	(200161)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9907741	A1	WO 1998-FR1730	19980803
FR 2767060	A1	FR 1997-10301	19970807
NO 9901558	A	WO 1998-FR1730	19980803
		NO 1999-1558	19990330
AU 9889875	A	AU 1998-89875	19980803
EP 948534	A1	EP 1998-941530	19980803
		WO 1998-FR1730	19980803
CN 1241193	A	CN 1998-801479	19980803
MX 9903186	A1	MX 1999-3186	19990406
JP 2001503068	W	WO 1998-FR1730	19980803
		JP 1999-511756	19980803
HU 2000001451	A2	WO 1998-FR1730	19980803
		HU 2000-1451	19980803
NZ 334992	A	NZ 1998-334992	19980803

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9889875	A	Based on	WO 9907741
EP 948534	A1	Based on	WO 9907741
JP 2001503068	W	Based on	WO 9907741
HU 2000001451	A2	Based on	WO 9907741

PRIORITY APPLN. INFO: FR 1997-10301 19970807
AB WO 9907741 A UPAB: 19991122
NOVELTY - Composition contains at least part of the low molecular weight subunit (**TbpB**) of the human transferrin receptor (hTR) from a specific strain of **Neisseria** meningitidis that contains **TbpB**-encoding DNA (I). DETAILED DESCRIPTION - (I) (a) contains two AvaII and three HincII restriction sites but no sites for VspI or XhoI or (preferably also) (b) generates a polymerase chain reaction (PCR) amplicon of 765-775, especially 772 (from strains of group BZ83) bp, using the primers P1 and P2: 5'-AAGACCAAGGCGGATACGGT4GC (P1) 5'-

GAAGACGAGTCGGAAACAAAGGGATG (P2). An INDEPENDENT CLAIM is also included for a composition containing (I).

USE - The compositions are used as **vaccines** for treatment or prevention of meningococcal infections, particularly meningitis.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Induction of an immune response.

ADVANTAGE - **TbpB** is from strains of the BZ83 group which have been the major cause of recent outbreaks of meningitis in many parts of the world.

Dwg.0/0

L125 ANSWER 54 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1997-235896 [21] WPIDS
DOC. NO. CPI: C1997-075698
TITLE: New subunit protein of **Neisseria** meningitidis human transferrin receptor - including a M982 type hinge region, also deletion mutants, useful as immunogenic components of broad spectrum **vaccines**.
DERWENT CLASS: B04 D16
INVENTOR(S): QUENTIN-MILLET, M; ROKBI, B; KANG LING, L; MAZARIN, V; QUENTIN, M M J
PATENT ASSIGNEE(S): (INMR) PASTEUR MERIEUX SERUMS & VACCINS; (INMR) PASTEUR MERIEUX SERUMS & VACCINS SA
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9713860	A1	19970417	(199721)*	FR	92
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA CN HU JP MX NO NZ US					
FR 2739624	A1	19970411	(199723)		80
AU 9672213	A	19970430	(199734)		
NO 9702314	A	19970718	(199739)		
EP 796332	A1	19970924	(199743)	FR	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
HU 9801714	A2	19981028	(199850)		
JP 11500630	W	19990119	(199913)		93
AU 720789	B	20000615	(200036)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9713860	A1	WO 1996-FR1580	19961010
FR 2739624	A1	FR 1995-12106	19951010
AU 9672213	A	AU 1996-72213	19961010
NO 9702314	A	WO 1996-FR1580	19961010
		NO 1997-2314	19970521
EP 796332	A1	EP 1996-933511	19961010
		WO 1996-FR1580	19961010
HU 9801714	A2	WO 1996-FR1580	19961010
		HU 1998-1714	19961010
JP 11500630	W	WO 1996-FR1580	19961010
		JP 1997-514773	19961010
AU 720789	B	AU 1996-72213	19961010

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 9672213	A	Based on	WO 9713860
EP 796332	A1	Based on	WO 9713860
HU 9801714	A2	Based on	WO 9713860
JP 11500630	W	Based on	WO 9713860
AU 720789	B	Previous Publ.	AU 9672213
		Based on	WO 9713860

PRIORITY APPLN. INFO: FR 1995-12106 19951010

AB WO 9713860 A UPAB: 19990416

New pure protein (I) is the lower molecular weight subunit, **Tbp2**, of the human transferrin receptor (HTR) of a strain of **Neisseria** meningitidis. This strain is not recognised in dot blots by antisera raised against the **Tbp2** polypeptide of N. meningitidis M982 having deletions (amino acids (aa) 362-379, 418-444, 465-481 and 500-520) in the hypervariable part of the second domain (hinge region). (I) is encoded by a DNA of about 2.1 kb (including a M982-type hinge region). Also new are: (1) polypeptides (Ia) able to bind to human transferrin and derived from (I) by deletion of one or more aa from the C terminus or within the first 40 aa, and (2) DNA encoding (I) and (Ia).

USE - (I) and (Ia), which generate neutralising antibodies, are used in **vaccines** for treatment or prevention of N. meningitidis infections.

ADVANTAGE - When (I) is included in **vaccines** together with known **Tbp2** subunits, the range of protection afforded by the **vaccine** is widened.

Dwg.0/5

L125 ANSWER 55 OF 57 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1996-030562 [03] WPIDS

DOC. NO. CPI: C1996-010537

TITLE: Polypeptide(s) for **vaccination** against **Neisseria** meningitidis group B - comprising deletion mutants of transferrin receptor **Tbp2** subunit.

DERWENT CLASS: B04 D16

INVENTOR(S): JACOBS, E; KANG, L; LEGRAIN, M; MAZARIN, V; QUENTIN, M B J; LISSOLO, L; MILLET, M B J

PATENT ASSIGNEE(S): (INMR) PASTEUR MERIEUX SERUMS & VACCINS SA; (TRGE) TRANSGENE SA; (INMR) PASTEUR MERIEUX SERUMS & VACCINS

COUNTRY COUNT: 24

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9533049	A2	19951207	(199603)*	EN	114
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA FI HU JP NO US					
FR 2720408	A1	19951201	(199604)		90
AU 9526757	A	19951221	(199612)		
NO 9600332	A	19960321	(199621)		
WO 9533049	A3	19960104	(199622)		
EP 720653	A1	19960710	(199632)	FR	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
FI 9600428	A	19960328	(199635)		
JP 09501059	W	19970204	(199715)		108
HU 75992	T	19970528	(199805)		
AU 706090	B	19990610	(199934)		
HU 220116	B	20011128	(200206)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9533049	A2	WO 1995-FR701	19950530
FR 2720408	A1	FR 1994-6594	19940531
AU 9526757	A	AU 1995-26757	19950530
NO 9600332	A	WO 1995-FR701	19950530
		NO 1996-332	19960126
WO 9533049	A3	WO 1995-FR701	19950530
EP 720653	A1	EP 1995-921860	19950530
		WO 1995-FR701	19950530
FI 9600428	A	WO 1995-FR701	19950530
		FI 1996-428	19960130
JP 09501059	W	WO 1995-FR701	19950530
		JP 1996-500434	19950530
HU 75992	T	WO 1995-FR701	19950530
		HU 1996-210	19950530
AU 706090	B	AU 1995-26757	19950530
HU 220116	B	WO 1995-FR701	19950530
		HU 1996-210	19950530

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9526757	A	Based on	WO 9533049
EP 720653	A1	Based on	WO 9533049
JP 09501059	W	Based on	WO 9533049
HU 75992	T	Based on	WO 9533049
AU 706090	B	Previous Publ.	AU 9526757
		Based on	WO 9533049
HU 220116	B	Previous Publ.	HU 75992
		Based on	WO 9533049

PRIORITY APPLN. INFO: FR 1994-6594 19940531

AB WO 9533049 A UPAB: 19960122

A new polypeptide has an amino acid sequence derived from that of the **Tbp2** subunit of the transferrin receptor of a **Neisseria** meningitidis strain of type IM2169 or type IM2394, notably by total or partial deletion of at least one domain of the said **Tbp2** subunit of type IM2169 or IM2394, provided that the first and second domains are not simultaneously and totally deleted; the first, second and third domains of **Tbp2** are defined by alignment with maximum homology on the sequence of the **Tbp2** subunit of the respective reference strain (i.e. IM2169 or IM2394), as shown in defined sequences of 2230 and 1808 bp given in the specification. Also claimed are: (1) an isolated DNA fragment coding for a polypeptide as above; and (2) a monoclonal antibody that is (i) capable of recognising an epitope present in the first domain of a **Tbp2** subunit of type IM2169 or IM2394, where the epitope has a sequence homologous to that present in the first domain of the **Tbp2** subunit of the IM2394 strain and is selected from YKGTW, EFEVDFSDKTIKGTL, EGGFYGPKGEEL and AVFGAK, and opt. (ii) incapable of recognising the epitope in the third domain whose sequence is homologous to the recognised sequence in the first domain.

USE - The polypeptide induces an immune response against N. meningitidis. The monoclonal antibodies are useful for treating a N. meningitidis infection by passive immunotherapy.

ADVANTAGE - Compsns. comprising the polypeptide are effective against infections by N. meningitidis strains of serogroup B, against which conventional polysaccharide **vaccines** are not effective.

Dwg.0/10

L125 ANSWER 56 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1995-075239 [10] WPIDS
DOC. NO. CPI: C1995-033499
TITLE: High expression of outer membrane **meningococcal** group B **porin** proteins - and fusion proteins in Escherichia coli, and purification method; for use in **vaccines** against **Neisseria meningitidis** and in research..
DERWENT CLASS: B04 D16
INVENTOR(S): BLAKE, M S; HRONOWSKI, L J J; LIANG, S; PULLEN, J K; QI, H L; TAI, J Y; HRONOWSKI, L J
PATENT ASSIGNEE(S): (NAVA-N) NORTH AMERICAN VACCINE INC; (UYRQ) UNIV ROCKEFELLER; (BAXT) BAXTER HEALTHCARE SA
COUNTRY COUNT: 57
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9503413	A1	19950202	(199510)*	EN	81
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE					
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KE KG KP KR KZ LK LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA UZ VN					
AU 9473716	A	19950220	(199521)		
US 5439808	A	19950808	(199537)		43
NO 9600256	A	19960320	(199621)		
EP 713530	A1	19960529	(199626)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
FI 9600309	A	19960322	(199635)		
BR 9407092	A	19960903	(199641)		
JP 09500538	W	19970121	(199713)		81
NZ 269996	A	19971024	(199749)		
US 5747287	A	19980505	(199825)		
AU 690570	B	19980430	(199829)		
AU 9876147	A	19981022	(199903)		
US 5879686	A	19990309	(199917)		
AU 711016	B	19991007	(199954)		
US 6013267	A	20000111	(200010)		
RU 2181378	C2	20020420	(200240)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9503413	A1		WO 1994-US8327	19940722
AU 9473716	A		AU 1994-73716	19940722
US 5439808	A		US 1993-96182	19930723
NO 9600256	A		WO 1994-US8327	19940722
			NO 1996-256	19960122
EP 713530	A1		EP 1994-922701	19940722
			WO 1994-US8327	19940722
FI 9600309	A		WO 1994-US8327	19940722
			FI 1996-309	19960123
BR 9407092	A		BR 1994-7092	19940722
			WO 1994-US8327	19940722
JP 09500538	W		WO 1994-US8327	19940722
			JP 1995-505354	19940722
NZ 269996	A		NZ 1994-269996	19940722
			WO 1994-US8327	19940722
US 5747287	A	Div ex	US 1993-96182	19930723
		Cont of	US 1995-431264	19950428

			US 1997-877109	19970617
AU 690570	B		AU 1994-73716	19940722
AU 9876147	A	Div ex	AU 1994-73716	19940722
			AU 1998-76147	19980714
US 5879686	A	Div ex	US 1993-96182	19930723
		Div ex	US 1995-431264	19950428
			US 1997-853504	19970508
AU 711016	B	Div ex	AU 1994-73716	19940722
			AU 1998-76147	19980714
US 6013267	A	Div ex	US 1993-96182	19930723
		Div ex	US 1995-431264	19950428
			US 1997-798760	19970211
RU 2181378	C2		WO 1994-US8327	19940722
			RU 1996-103644	19940722

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9473716	A	Based on	WO 9503413
EP 713530	A1	Based on	WO 9503413
BR 9407092	A	Based on	WO 9503413
JP 09500538	W	Based on	WO 9503413
NZ 269996	A	Based on	WO 9503413
US 5747287	A	Cont of	US 5439808
AU 690570	B	Previous Publ.	AU 9473716
		Based on	WO 9503413
US 5879686	A	Div ex	US 5439808
AU 711016	B	Div ex	AU 690570
		Previous Publ.	AU 9876147
US 6013267	A	Div ex	US 5439808
RU 2181378	C2	Based on	WO 9503413

PRIORITY APPLN. INFO: US 1993-96182 19930723; US 1995-431264 19950428; US 1997-877109 19970617; US 1997-853504 19970508; US 1997-798760 19970211

AB WO 9503413 A UPAB: 19950314

A new method for the high level expression of outer membrane meningococcal gp B **porin** protein (PP) or fusion protein in Escherichia coli comprises: (i) transforming into E. coli a vector contg. a selectable marker and a gene encoding a mature PP (mPP) or a fusion of mPP to amino acids 1-22 of the T7 gene phi10 capsid protein, where the gene is operably linked to the T7 promoter; (ii) growing the E. coli in selection medium; and (iii) inducing expression of the protein in E. coli, where the protein comprises greater than 2% of the total protein expressed.

USE - The protein may be used in **vaccines** against **Neisseria** menigitidis.

ADVANTAGE - The large amounts of protein produced and easier genetic manipulation enable more detailed research on PPs and **vaccines**.

Dwg.0/11

L125 ANSWER 57 OF 57 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1990-348267 [46] WPIDS
DOC. NO. CPI: C1990-151153
TITLE: Isolation and purificn. of transferrin receptor proteins - used in **vaccine** antigens against bacterial pathogens, e.g. **Neisseria**.
DERWENT CLASS: B04 D16
INVENTOR(S): SCHRYVERS, A B
PATENT ASSIGNEE(S): (SCHR-I) SCHRYVERS A B; (UYTE-N) UNIV TECHNOLOGIES INT INC; (SCHR-I) SCHRIVERS A B; (UYTE-N) UNIV TECHN INT INC;

(UYTE-N) UNIVERSITIES TECHNOLOGIES INT INC; (UNIW) UNIV WASHINGTON

COUNTRY COUNT: 22

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9012591	A	19901101	(199046)*		34
RW: AT BE CH DE DK ES FR GB IT LU NL SE					
W: AU CA JP KR SU					
AU 9055261	A	19901116	(199107)		
ZA 9003234	A	19910227	(199114)		
US 5141743	A	19920825	(199237)		9
JP 04506794	W	19921126	(199302)		16
EP 528787	A1	19930303	(199309)	EN	34
R: AT BE CH DE DK ES FR GB IT LI LU NL SE					
NZ 233471	A	19931125	(199350)		
US 5292869	A	19940308	(199410)		9
AU 649950	B	19940609	(199428)		
NZ 247967	A	19950224	(199513)		
EP 528787	B1	19981202	(199901)	EN	
R: AT BE CH DE DK ES FR GB IT LI LU NL SE					
DE 69032806	E	19990114	(199908)		
ES 2127184	T3	19990416	(199922)		
CA 2051808	C	19991214	(200018)	EN	
US 6060058	A	20000509	(200030)		
IL 94228	A	20010319	(200129)		
KR 240974	B1	20000801	(200131)		
JP 3335622	B2	20021021	(200272)		15
IL 127163	A	20021110	(200282)		
JP 2002316942	A	20021031	(200304)		11

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
ZA 9003234	A		ZA 1990-3234	19900427
US 5141743	A	Cont of	US 1989-344356	19890427
			US 1991-639365	19910110
JP 04506794	W		JP 1990-506296	19900426
			WO 1990-CA131	19900426
EP 528787	A1		EP 1990-906093	19900426
			WO 1990-CA131	19900426
NZ 233471	A		NZ 1990-233471	19900427
US 5292869	A	CIP of	US 1989-344356	19890427
			US 1990-507481	19900411
AU 649950	B		AU 1990-55261	19900426
NZ 247967	A		NZ 1990-247967	19900427
EP 528787	B1		EP 1990-906093	19900426
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DE 69032806	E		DE 1990-632806	19900426
			EP 1990-906093	19900426
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ES 2127184	T3		EP 1990-906093	19900426
CA 2051808	C		CA 1990-2051808	19900426
			WO 1990-CA131	19900426
US 6060058	A	Cont of	US 1989-344356	19890427
		Div ex	US 1991-639365	19910110
		Cont of	US 1992-851005	19920312
		Cont of	US 1994-207719	19940309
			US 1995-483881	19950607

IL 94228	A		IL 1990-94228	19900427
KR 240974	B1		WO 1990-CA131	19900426
			KR 1991-701442	19911025
JP 3335622	B2		JP 1990-506296	19900426
			WO 1990-CA131	19900426
IL 127163	A	Div ex	IL 1990-94228	19900427
			IL 1990-127163	19900427
JP 2002316942	A	Div ex	JP 1990-506296	19900426
			JP 2002-54731	19900426

FILING DETAILS:

PATENT NO	KIND		PATENT NO
JP 04506794	W	Based on	WO 9012591
EP 528787	A1	Based on	WO 9012591
AU 649950	B	Previous Publ.	AU 9055261
		Based on	WO 9012591
NZ 247967	A	Div ex	NZ 233471
EP 528787	B1	Based on	WO 9012591
DE 69032806	E	Based on	EP 528787
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ES 2127184	T3	Based on	EP 528787
CA 2051808	C	Based on	WO 9012591
US 6060058	A	Div ex	US 5141743
JP 3335622	B2	Previous Publ.	JP 04506794
		Based on	WO 9012591
IL 127163	A	Div ex	IL 94228

PRIORITY APPLN. INFO: US 1990-507481 19900411; US 1989-344356 19890427; US 1991-639365 19910110; US 1992-851005 19920312; US 1994-207719 19940309; US 1995-483881 19950607

AB WO 9012591 A UPAB: 19990127

The method comprises: (i) isolating an iron deficient membrane preparation from a bacterial strain expressing **transferrin-binding** activity; (ii) binding a biotinylated derivative of transferrin to the membrane; and (iii) isolating the transferrin receptor protein (A) by affinity chromatography with immobilised streptavidin or avidin.

Also claimed is (a) (A); (b) a method as above for isolating lactoferrin receptor protein (B); (c) (B); and (d) a **vaccine** antigen containing (A) and/or (B). The bacterial strain is e.g. **Neisseria** meningitis, Haemophilus influenzae etc. (47 strains given).

USE/ADVANTAGE - The **vaccine** antigens exhibit superior immunological memory to current polysaccharide capsular **vaccines** ; they are effective against bacterial pathogens that acquire iron directly through transferrin and/or lactoferrin receptors. The antigens are also suitable for providing immunity to young children.

In an example to evaluate expression regulation of lactoferrin, binding activity in N. meningitis, strain B16B6 was grown in both containing a variety of different additions. Human lactoferrin conjugated to peroxidase (HRP-loctoferrin) was used to detect the activity. Addition of the synthetic iron chelator EDDA markedly increased the activity in cells grown in both along. Near-maximal levels of expression were achieved with intermediate levels of added EDDA.

Dwg.0/1

=> file home
FILE 'HOME' ENTERED AT 15:57:58 ON 18 APR 2003

National Library of Medicine - Medical Subject Headings

2003 MeSH

MeSH Supplementary Concept Data

Return to Entry Page

Name of Substance	NspA protein
Record Type	C
Registry Number	0
Entry Term	nspA gene product
Heading Mapped to	*Bacterial Outer Membrane Proteins
Indexing Information	Antigens, Bacterial
Source	J Exp Med 1997 Apr 7;185(7):1173-83
Frequency	8
Note	candidate for vaccine against meningococcal infection; isolated from Neisseria meningitidis; amino acid sequence in first source; GenBank U52066
Date of Entry	19970509
Revision Date	20010223
Unique ID	C105506

Return to Entry Page **Link to NLM Cataloging Classification**

LOCUS NP_283654 174 aa linear BCT 10-DEC-2002
DEFINITION outer membrane protein [Neisseria meningitidis Z2491].
ACCESSION NP_283654
VERSION NP_283654.1 GI:15793832
DBSOURCE REFSEQ: accession NC_003116.1
KEYWORDS
SOURCE Neisseria meningitidis Z2491
ORGANISM Neisseria meningitidis Z2491
Bacteria; Proteobacteria; Betaproteobacteria; Neisseriales;
Neisseriaceae; Neisseria.
REFERENCE 1 (residues 1 to 174)
AUTHORS Parkhill,J., Achtman,M., James,K.D., Bentley,S.D., Churcher,C.,
Klee,S.R., Morelli,G., Basham,D., Brown,D., Chillingworth,T.,
Davies,R.M., Davis,P., Devlin,K., Feltwell,T., Hamlin,N.,
Holroyd,S., Jagels,K., Leather,S., Moule,S., Mungall,K.,
Quail,M.A., Rajandream,M.A., Rutherford,K.M., Simmonds,M.,
Skelton,J., Whitehead,S., Spratt,B.G. and Barrell,B.G.
TITLE Complete DNA sequence of a serogroup A strain of Neisseria
meningitidis Z2491
JOURNAL Nature 404 (6777), 502-506 (2000)
MEDLINE 20222556
PUBMED 10761919
REFERENCE 2 (residues 1 to 174)
AUTHORS NCBI Microbial Genomes Annotation Project.
TITLE Direct Submission
JOURNAL Submitted (26-SEP-2001) National Center for Biotechnology
Information, NIH, Bethesda, MD 20894, USA
COMMENT PROVISIONAL REFSEQ: This record has not yet been subject to final
NCBI review. The reference sequence was derived from CAB84143.
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/note="nspA, outer membrane protein, len: 174 aa; highly
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Neisseria meningitidis strain 608B outer membrane protein
precursor (174 aa), fasta scores; E(): 0, 98.3% identity
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Similar to NMA1890, NMA2043 and NMA1676, which contain
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VERSION CAB84143.1 GI:7379578
DBSOURCE embl locus NMA3Z2491, accession AL162754.2
KEYWORDS .
SOURCE Neisseria meningitidis Z2491
ORGANISM Neisseria meningitidis Z2491
Bacteria; Proteobacteria; Betaproteobacteria; Neisseriales;
Neisseriaceae; Neisseria.
REFERENCE 1 (residues 1 to 174)
AUTHORS Parkhill,J., Achtman,M., James,K.D., Bentley,S.D., Churcher,C.,
Klee,S.R., Morelli,G., Basham,D., Brown,D., Chillingworth,T.,
Davies,R.M., Davis,P., Devlin,K., Feltwell,T., Hamlin,N.,
Holroyd,S., Jagels,K., Leather,S., Moule,S., Mungall,K.,
Quail,M.A., Rajandream,M.A., Rutherford,K.M., Simmonds,M.,
Skelton,J., Whitehead,S., Spratt,B.G. and Barrell,B.G.
TITLE Complete DNA sequence of a serogroup A strain of Neisseria
meningitidis Z2491
JOURNAL Nature 404 (6777), 502-506 (2000)
MEDLINE 20222556
PUBMED 10761919
REFERENCE 2 (residues 1 to 174)
AUTHORS Parkhill,J.
TITLE Direct Submission
JOURNAL Submitted (30-MAR-2000) Submitted on behalf of the Neisseria
sequencing team, Sanger Centre, Wellcome Trust Genome Campus,
Hinxton, Cambridge CB10 1SA E-mail: parkhill@sanger.ac.uk
COMMENT Notes:
Details of N. meningitidis sequencing at the Sanger Centre are
available on the World Wide Web.
(URL, http://www.sanger.ac.uk/Projects/N_meningitidis/).
FEATURES Location/Qualifiers
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highly similar to surface antigens from other Neisseria
meningitidis isolates e.g. TR:P96943 (EMBL:U52066)
Neisseria meningitidis strain 608B outer membrane protein
precursor (174 aa), fasta scores; E(): 0, 98.3% identity
in 174 aa overlap. Contains an N-terminal signal sequence.
Similar to NMA1890, NMA2043 and NMA1676, which contain
short indels with respect to nspA"
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121 sqtstglgvl agvsyavtpn vdldagyryn yigkvntvkn vrsgelsagv rvkf
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Revised: July 5, 2002.